

# Posicionamiento terapéutico para el tratamiento farmacológico del cáncer de próstata

**Entrega N. 4: Anexos**

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14 de noviembre de 2025



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## Agradecimientos

El Instituto de Evaluación Tecnológica en Salud (IETS) expresa su agradecimiento a todas las personas e instituciones que participaron en el desarrollo de este documento. Su compromiso, conocimiento y experiencia fueron fundamentales para fortalecer el rigor técnico y la relevancia de los resultados presentados, contribuyendo al propósito común de mejorar la calidad, la equidad y la sostenibilidad del sistema de salud en Colombia.

- Asociación Colombiana de Hematología y Oncología
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## Citación

Ministerio de Salud y Protección Social e Instituto de Evaluación Tecnológica en Salud - IETS. Posicionamiento terapéutico para el tratamiento farmacológico del cáncer de próstata. 1a edición. Bogotá D.C.: Instituto de Evaluación Tecnológica en Salud (IETS); 2025.

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## Fuente de financiación

El presente documento fue financiado por el Ministerio de Salud y Protección Social mediante el contrato Interadministrativo No. MPSP-1497 de 2025, el cual fue suscrito entre el Ministerio de Salud y Protección Social y el IETS.

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## Lista de abreviaturas

|        |                                                                                        |
|--------|----------------------------------------------------------------------------------------|
| 3DCRT  | Radioterapia conformacional tridimensional                                             |
| CT     | Tomografía computarizada                                                               |
| DES    | Dietilestilbestrol                                                                     |
| EA     | Evento adverso                                                                         |
| ECA    | Ensayo clínico aleatorizado                                                            |
| EPID   | Dispositivo electrónico de imagen portal                                               |
| FDA    | Administración de Alimentos y Medicamentos de los Estados Unidos                       |
| GPC    | Guía de Práctica Clínica                                                               |
| GRADE  | Sistema de clasificación de la calidad de la evidencia y fuerza de las recomendaciones |
| GnRH   | Hormona liberadora de gonadotropinas                                                   |
| HR     | Razón de riesgo                                                                        |
| HRQoL  | Calidad de vida relacionada con la salud                                               |
| HTA    | Evaluación de tecnologías en salud                                                     |
| ICER   | Razón incremental de costo-efectividad                                                 |
| IETS   | Instituto de Evaluación Tecnológica en Salud                                           |
| INC    | Instituto Nacional de Cancerología                                                     |
| INS    | Instituto Nacional de Salud                                                            |
| INVIMA | Instituto Nacional de Vigilancia de Medicamentos y Alimentos                           |
| LHRH   | Hormona liberadora de la hormona luteinizante                                          |
| LILACS | Literatura Latinoamericana y del Caribe en Ciencias de la Salud                        |
| MFS    | Supervivencia libre de metástasis                                                      |
| MRI    | Imagen por resonancia magnética                                                        |
| MSPS   | Ministerio de Salud y Protección Social                                                |
| OMS    | Organización Mundial de la Salud                                                       |
| OR     | Razón de probabilidades                                                                |
| ORR    | Tasa de respuesta objetiva                                                             |
| OS     | Supervivencia global                                                                   |
| PARP   | Poli(ADP-ribosa) polimerasa (inhibidor de PARP)                                        |
| PFS    | Supervivencia libre de progresión                                                      |
| PRISMA | Elementos de referencia para informes de revisiones sistemáticas y metaanálisis        |
| PSA    | Antígeno prostático específico                                                         |
| PT     | Posicionamiento terapéutico                                                            |
| QoL    | Calidad de vida                                                                        |
| RWD    | Datos del mundo real                                                                   |
| RWE    | Evidencia del mundo real                                                               |
| RT     | Radioterapia                                                                           |



|        |                                                              |
|--------|--------------------------------------------------------------|
| RTVSS  | Registro de Transferencias de Valor del Sector Salud         |
| SAE    | Evento adverso grave                                         |
| SGSSS  | Sistema General de Seguridad Social en Salud                 |
| TPA    | Terapia de privación androgénica                             |
| TRAES  | Eventos adversos relacionados con el tratamiento             |
| UNIRS  | Unidad de Información y Referencia en Salud                  |
| mCRPC  | Cáncer de próstata metastásico resistente a la castración    |
| mHSPC  | Cáncer de próstata metastásico sensible a las hormonas       |
| nmCRPC | Cáncer de próstata no metastásico resistente a la castración |



## Anexo A. Preguntas de investigación inicial

### Anexo A.1 Preguntas de investigación inicial (Primera sesión)

#### Pregunta 1:

¿En pacientes con diagnóstico de cáncer de próstata localmente avanzado o regional, cuál es la efectividad y seguridad de la terapia de privación de andrógenos (TPA) combinado con radioterapia?

|              |                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                      |
|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Población    | Pacientes masculinos adultos (>18 años) con diagnóstico de cáncer de próstata localmente avanzado (N0, M0) o regional (N1, M0)                                                                                                                                                                                                                                                                   |                                                                                                                                                                      |
| Intervención | Radioterapia + cualquiera de los siguientes TPA                                                                                                                                                                                                                                                                                                                                                  | Radioterapia + cualquiera de los siguientes TPA con antiandrógenos                                                                                                   |
|              | Goserelina<br>Leuprorelina<br>Triptorelina<br>Degarelix                                                                                                                                                                                                                                                                                                                                          | Goserelina + bicalutamida<br>Leuprorelina + bicalutamida<br>Triptorelina + bicalutamida<br>Degarelix + bicalutamida                                                  |
| Comparador   | Entre ellos o terapia estándar/placebo*                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                      |
| Desenlaces   | Eficacia <ul style="list-style-type: none"><li>• Supervivencia global (OS)</li><li>• Supervivencia libre de progresión (PFS)</li><li>• Supervivencia libre de metástasis (MFS)</li><li>• Supervivencia libre de progresión bioquímica – PSA-</li><li>• Tasa de respuesta objetiva (ORR)</li><li>• Tasa de respuesta del PSA</li><li>• Calidad de vida relacionada con la salud (HRQoL)</li></ul> | Seguridad <ul style="list-style-type: none"><li>• Eventos adversos totales</li><li>• EA graves (SAEs)</li><li>• EA relacionados con el tratamiento (TRAEs)</li></ul> |
| Estudios     | Revisiones sistemáticas de la literatura y ensayos clínicos aleatorios controlados                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                      |

*\*El cuidado estándar (vigilancia activa, prostatectomía radical o radioterapia sin tratamiento farmacológico) y el placebo no serán objeto de posicionamiento terapéutico en este documento. No obstante, se considerarán estudios con estos comparadores en caso de ser*

necesarios como nodos dentro de un posible metaanálisis en red. Fuente: elaboración propia.

## Pregunta 2:

¿En pacientes con diagnóstico de CP no metastásico resistente a castración, cuál es la efectividad y seguridad de la terapia farmacológica intensificada (TPA con antiandrógenos)?

|                     |                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                 |
|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Población</b>    | Pacientes masculinos adultos (>18 años) con diagnóstico de cáncer de próstata no metastásico resistente a (nmCRPC)                                                                                                                                                                                          |                                                                                                                                                                                 |
| <b>Intervención</b> | <b>Continuar TPA e intensificar tratamiento con uno de los siguientes antiandrógenos:</b>                                                                                                                                                                                                                   |                                                                                                                                                                                 |
|                     | <ul style="list-style-type: none"> <li>• Bicalutamida</li> <li>• Apalutamida</li> </ul>                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>• Enzalutamida</li> <li>• Darolutamida</li> </ul>                                                                                        |
| <b>Comparador</b>   | Entre ellos o terapia estándar/placebo*                                                                                                                                                                                                                                                                     |                                                                                                                                                                                 |
| <b>Desenlaces</b>   | <b>Eficacia</b> <ul style="list-style-type: none"> <li>• Supervivencia global (OS)</li> <li>• Supervivencia libre de progresión (PFS)</li> <li>• Supervivencia libre de metástasis (MFS)</li> <li>• Tasa de respuesta objetiva (ORR)</li> <li>• Calidad de vida relacionada con la salud (HRQoL)</li> </ul> | <b>Seguridad</b> <ul style="list-style-type: none"> <li>• Eventos adversos totales</li> <li>• EA graves (SAEs)</li> <li>• EA relacionados con el tratamiento (TRAEs)</li> </ul> |
| <b>Estudios</b>     | Revisiones sistemáticas de la literatura y ensayos clínicos aleatorios controlados                                                                                                                                                                                                                          |                                                                                                                                                                                 |

\*El cuidado estándar (TPA o TPA + antiandrógenos de 1ra Generación) y el placebo no serán objeto de posicionamiento terapéutico en este documento. No obstante, se considerarán estudios con estos comparadores en caso de ser necesarios como nodos dentro de un posible metaanálisis en red. Notas aclaratorias: 1) Se debe mantener el mismo análogo de GnRH (goserelina, triptorelina, leuprorelina) utilizado en la fase hormono-sensible, por lo cual, se recomienda continuar con igual manejo de primera línea de fondo



### Pregunta 3:

¿En pacientes con diagnóstico de **CP metastásico sensible a hormonas**, cuál es la efectividad y seguridad de la terapia farmacológica combinada (TPA con antiandrógenos y/o abiraterona más prednisona)?

|                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                     |                                                                                                                                                                |                                                                                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| Población                                                                                                                                                                                                                                                                                                                                                                 | Pacientes masculinos adultos (>18 años) con diagnóstico de cáncer de próstata metastásico hormonosensible (mHSPC)                                                                                                                                                                                                                 |                                                                                                                                                     |                                                                                                                                                                |                                                                                                                                      |
| Intervención                                                                                                                                                                                                                                                                                                                                                              | TPA + antiandrógenos                                                                                                                                                                                                                                                                                                              |                                                                                                                                                     |                                                                                                                                                                |                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                           | Goserelina + bicalutamida<br>Goserelina + flutamida<br>Goserelina + apalutamida<br>Goserelina + enzalutamida<br>Goserelina + abiraterona*                                                                                                                                                                                         | Leuprorelina + bicalutamida<br>Leuprorelina + flutamida<br>Leuprorelina + apalutamida<br>Leuprorelina + enzalutamida<br>Leuprorelina + abiraterona* | Triptorelina + bicalutamida<br>Triptorelina + flutamida<br>Triptorelina + apalutamida<br>Triptorelina + enzalutamida<br>Triptorelina + abiraterona*            | Degarelix + bicalutamida<br>Degarelix + flutamida<br>Degarelix + apalutamida<br>Degarelix + enzalutamida<br>Degarelix + abiraterona* |
| Comparador                                                                                                                                                                                                                                                                                                                                                                | Entre ellos o terapia estándar/placebo                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |                                                                                                                                                                |                                                                                                                                      |
| Desenlaces                                                                                                                                                                                                                                                                                                                                                                | Eficacia <ul style="list-style-type: none"><li>Supervivencia global (OS)</li><li>Supervivencia libre de progresión (PFS)</li><li>Supervivencia libre de progresión bioquímica –PSA–</li><li>Tasa de respuesta objetiva (ORR)</li><li>Tasa de respuesta del PSA</li><li>Calidad de vida relacionada con la salud (HRQoL)</li></ul> |                                                                                                                                                     | Seguridad <ul style="list-style-type: none"><li>Eventos adversos totales</li><li>EA graves (SAEs)</li><li>EA relacionados con el tratamiento (TRAEs)</li></ul> |                                                                                                                                      |
|                                                                                                                                                                                                                                                                                                                                                                           | Revisiones sistemáticas de la literatura y ensayos clínicos aleatorios controlados                                                                                                                                                                                                                                                |                                                                                                                                                     |                                                                                                                                                                |                                                                                                                                      |
| *El cuidado estándar (TPA o TPA + Placebo no serán objeto de posicionamiento terapéutico en este documento. No obstante, se considerarán estudios con estos comparadores en caso de ser necesarios como nodos dentro de un posible metaanálisis en red. ‡ En todos los esquemas que incluyen abiraterona, se considera la coadministración con prednisona o prednisolona. |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                     |                                                                                                                                                                |                                                                                                                                      |

#### Pregunta 4:

¿En pacientes con diagnóstico de **CP metastásico resistente a castración**, cuál es la efectividad y seguridad de la terapia farmacológica combinada de segunda línea?

|                     |                                                                                                                                                                                                                                                                                                                                                                                        |                                                                  |
|---------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| <b>Población</b>    | Pacientes masculinos adultos (>18 años) con diagnóstico de cáncer de próstata metastásico resistente a castración (mCRPC)                                                                                                                                                                                                                                                              |                                                                  |
| <b>Intervención</b> | <b>Continuar TPA previa y adicionar quimioterapia</b>                                                                                                                                                                                                                                                                                                                                  |                                                                  |
|                     | Docetaxel<br>Cabazitaxel *<br>Mitoxantrona                                                                                                                                                                                                                                                                                                                                             |                                                                  |
|                     | <b>Continuar TPA previa y cambiar antiandrógenos</b>                                                                                                                                                                                                                                                                                                                                   |                                                                  |
|                     | Flutamida<br>Bicalutamida<br>Enzalutamida<br>Abiraterona*                                                                                                                                                                                                                                                                                                                              |                                                                  |
|                     | <b>Continuar TPA previa y adicionar quimioterapia + antiandrógenos</b>                                                                                                                                                                                                                                                                                                                 |                                                                  |
|                     | Docetaxel + flutamida<br>Cabazitaxel* + flutamida<br>Docetaxel + enzalutamida<br>Cabazitaxel* + enzalutamida<br>Docetaxel + abiraterona*<br>Cabazitaxel* + abiraterona*                                                                                                                                                                                                                |                                                                  |
|                     | <b>TPA + inhibidores de PARP</b>                                                                                                                                                                                                                                                                                                                                                       |                                                                  |
|                     | Olaparib                                                                                                                                                                                                                                                                                                                                                                               |                                                                  |
|                     | <b>Radiofármacos</b>                                                                                                                                                                                                                                                                                                                                                                   |                                                                  |
|                     | Radio-223 o Lutecio-177                                                                                                                                                                                                                                                                                                                                                                |                                                                  |
| <b>Comparador</b>   | Entre ellos o terapia estándar                                                                                                                                                                                                                                                                                                                                                         |                                                                  |
| <b>Desenlaces</b>   | <b>Eficacia</b><br>Supervivencia global (OS)<br>Supervivencia libre de progresión (PFS)<br>Tasa de respuesta objetiva (ORR)<br>Calidad de vida relacionada con la salud (HRQoL)                                                                                                                                                                                                        | <b>Seguridad</b><br>Eventos adversos totales<br>EA graves (SAEs) |
|                     | <p>* En todos los esquemas que incluyen cabazitaxel o abiraterona, se considera la coadministración con prednisona o prednisolona.</p> <p><b>Notas aclaratorias:</b> 1) Se debe mantener el mismo análogo de GnRH (goserelina, triptorelina, leuprorelina) utilizado en la fase hormono-sensible, por lo cual, se recomienda continuar con igual manejo de primera línea de fondo.</p> |                                                                  |

## **Anexo B. Espacios de participación**

### **Anexo B.1 Informe de conformación del grupo desarrollador, mapeo de los actores y convocatoria a espacios participativos**

#### **1. Introducción**

La participación en salud, al ser interdependiente de la realización efectiva del derecho a la salud, permite a los diferentes actores sociales asumir la responsabilidad y el compromiso de hacer parte de las deliberaciones y discusiones sobre los problemas en salud que los afectan (1).

En este marco, el IETS favorece el involucramiento de actores en los proyectos que ejecuta, pues configura una participación muy importante, en la medida en que los espacios de deliberación con las partes interesadas son clave para la obtención de datos relevantes en la definición de aspectos centrales del proceso y que no son necesariamente identificables en la literatura (2). En términos generales, se espera que los expertos aporten datos cuantitativos, cualitativos, experiencia y conocimiento derivado de la práctica alrededor del tema en particular (3) que orienten los procesos de toma de decisiones en salud (2).

Para el caso específico del posicionamiento terapéutico para el tratamiento del cáncer de próstata, el involucramiento de los expertos se hizo de manera incremental, es decir, se dio inicio con la conformación del equipo o del grupo desarrollador (GD) y se cerró con la convocatoria a espacios participativos de deliberación y definición del posicionamiento.

En este punto, es necesario mencionar que los actores que participan en el PT deben ser expertos y prescriptores del uso de medicamentos para el tratamiento de la condición de salud en tanto se requiere de su experiencia clínica para el desarrollo del PT (4).

Teniendo en cuenta lo anterior, el presente informe describe de manera sintética el proceso de gestión de espacios participativos adelantado en el marco de la construcción del posicionamiento terapéutico.

## **2. Metodología de convocatoria**

### **2.1 Mapeo de los actores**

Todo proceso de gestión de espacios participativos comienza con un mapeo de actores involucrados, de acuerdo con la Red Europea de Evaluación de Tecnologías (EUnetHTA, por su sigla en inglés). Se entiende por actores aquellos que corresponden a individuos, grupos u organizaciones que pueden proveer información relevante sobre la perspectiva de los grupos que representan y que serán afectados por la decisión; también son grupos u organizaciones que pueden, en un rol consultivo, contribuir a las acciones u objetivos de una organización, proyecto o política en salud (5).

En este contexto, para el posicionamiento en referencia, el mapeo o identificación de los actores clave se desarrolló conforme el objetivo del involucramiento (orientado a profesionales clínicos que tratan la condición y que prescriben medicamentos) y la temática. Este mapeo también fue presentado y complementado por el Ministerio de Salud y Protección Social.

En el primer momento del mapeo, es decir para la conformación del GD, y dada la necesidad de contar con expertos en el manejo de la condición de salud, se acudió a las siguientes sociedades científicas:

- Asociación Colombiana de Hematología y Oncología
- Asociación Colombiana de Radiología Oncológica
- Sociedad Colombiana de Urología
- Sociedad Colombiana de Medicina Familiar

Dada la urgencia de contar rápidamente los especialistas clínicos necesarios para el grupo desarrollador, también se contactaron profesionales independientes que expresaran su voluntad de hacer parte del proceso. En el transcurso del proceso, y considerando la complejidad en el abordaje del cáncer de próstata y la escasez de supra especialistas en el tema con voluntad de participar en el proceso, se desarrolló el ajuste metodológico necesario para involucrar a expertos con potenciales conflictos, reduciendo el riesgo de su materialización (este punto se explica con más detalle en la gestión de conflictos de intereses). Así, el grupo desarrollador final, quedó conformado de la siguiente manera:

**Tabla B-1. Expertos clínicos del grupo desarrollador**

| Organización que delega                                                               | Delegado                       | Perfil                                                                                                                                                                                                               |
|---------------------------------------------------------------------------------------|--------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Asociación Colombiana de Hematología y Oncología                                      | Herney Andrés García Perdomo   | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Magíster en epidemiología clínica. Doctor en educación. Doctor en ciencias biomédicas. Doctor en medicina clínica y salud pública. |
|                                                                                       | Ray Antonio Manneh Kopp        | Médico y cirujano. Especialista en oncología clínica. Máster en oncología molecular.                                                                                                                                 |
| Asociación Colombiana de Hematología y Oncología / Instituto Nacional de Cancerología | Martín Ignacio Zapata Laguado  | Médico y cirujano. Especialista en medicina interna. Especialista en oncología clínica. Especialista en epidemiología clínica. Máster en oncología molecular.                                                        |
| Instituto Nacional de Cancerología                                                    | Germán Fabián Godoy Pérez      | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Especialista en educación para profesionales de la salud.                                                                          |
|                                                                                       | Humberto Varela Ramírez        | Médico y cirujano. Especialista en medicina nuclear.                                                                                                                                                                 |
| Sociedad Colombiana de Medicina Familiar                                              | Diego Alfonso Beltrán Martínez | Médico y cirujano. Especialista en medicina familiar. Especialista en docencia universitaria. Magíster en epidemiología.                                                                                             |
| Asociación Colombiana de Radioterapia                                                 | Ramiro David Bermúdez Iguarán  | Médico y cirujano. Especialista en oncología radioterápica. Magíster en radiocirugía y radioterapia. Magíster en epidemiología clínica.                                                                              |
|                                                                                       | Lina María Loaiza Salazar      | Médica y cirujana. Especialista en oncología radioterápica. Máster en cuidados paliativos. Actual presidente de la Sociedad.                                                                                         |

Fuente: elaboración propia.

De cara al proceso de socialización y refinamiento de las preguntas de investigación tanto de efectividad y seguridad, como del componente económico, y al proceso de socialización de la evidencia y de definición del posicionamiento, se amplió el mapeo de actores. En la siguiente tabla se ilustran las partes interesadas que se mapearon y posteriormente se convocaron para su participación en este momento de construcción del posicionamiento:

**Tabla B-2. Mapeo de actores para espacios participativos**

| Tipo de actor                           | Organización por convocar                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sociedades científicas                  | <ul style="list-style-type: none"> <li>Asociación Colombiana de Hematología y Oncología</li> <li>Asociación Colombiana de Radiología Oncológica</li> <li>Sociedad Colombiana de Urología</li> <li>Sociedad Colombiana de Medicina Familiar</li> </ul>                                                                                                                                                                                                                                  |
| Instituciones Prestadoras de Salud      | <ul style="list-style-type: none"> <li>Instituto Nacional de Cancerología</li> <li>Centro Javeriano de Oncología</li> <li>Fundación Centro de Tratamiento e Investigación sobre cáncer (CTIC)</li> <li>Liga Colombiana contra el Cáncer</li> <li>Clínica Oncológica de Salud de Colsubsidio</li> <li>Clínica Universitaria Colombia</li> <li>Fundación Santa Fe de Bogotá</li> <li>Clínica Los Nogales</li> <li>Fundación Valle de Lili</li> <li>Hospital Pablo Tobón Uribe</li> </ul> |
| Ministerio de Salud y Protección Social | <ul style="list-style-type: none"> <li>Dirección de Beneficios, Costos y Tarifas</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                            |

Fuente: elaboración propia.

Adicionalmente, se buscaron 13 expertos independientes que han participado previamente en procesos del IETS, para invitarles a participar. En la siguiente sección se relacionan los participantes que finalmente aceptaron involucrarse en el proceso.

Por otro lado, en lo que respecta a los referentes técnicos del Ministerio de Salud y Protección Social, en la siguiente tabla se ilustran los delegados del proceso:

**Tabla B-3. Delegados del Ministerio de Salud y Protección Social**

| Dependencia                                                                        | Delegado                        | Perfil                                                                                                      |
|------------------------------------------------------------------------------------|---------------------------------|-------------------------------------------------------------------------------------------------------------|
| Dirección de Regulación de Beneficios, Costos y Tarifas del Aseguramiento en Salud | Enrique Alejandro Robayo Duarte | Químico farmacéutico. Especialista en dirección y gestión de proyectos. Magíster (c) en políticas públicas. |
|                                                                                    | Inés María Galindo Henríquez    | Médica y cirujana. Especialista en epidemiología.                                                           |
|                                                                                    | David Eduardo Gómez Lizarazu    | Economista. Magíster en estadística.                                                                        |

Fuente: elaboración propia.

De parte del IETS, el equipo metodológico se conformó de la siguiente manera:

**Tabla B-4. Expertos metodólogos del grupo desarrollador del IETS**

| Nombre                              | Rol                                                                                                          |
|-------------------------------------|--------------------------------------------------------------------------------------------------------------|
| Sandra Johanna Echeverry Coral      | Epidemióloga de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.               |
| Jefferson Antonio Buendía Rodríguez | Epidemiólogo y coordinador de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. |
| Juan Camilo Martínez Molina         | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.               |
| Lucas López Quiceno                 | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.               |
| Grey Yuliet Ceballos García         | Economista de la Unidad de economía de la salud y analítica en salud.                                        |
| Angélica Ordóñez Aristizábal        | Economista de la Unidad de economía de la salud y analítica en salud.                                        |
| Juan Sebastián Ortiz Ramírez        | Economista de la Unidad de economía de la salud y analítica en salud.                                        |
| Gilberto Andrés Morales Zamora      | Analítico de la Unidad de economía de la salud y analítica en salud.                                         |
| Anamaría García                     | Física y analítica de la de la Unidad de economía de la salud y analítica en salud.                          |
| María Camila Tavera                 | Ingeniera biomédica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.        |
| Diana Marcela Segura Sandino        | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.       |
| Suleidy Angarita Arévalo            | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.       |
| Fanny Emelina Torres García         | Profesional de apoyo a participación de la Jefatura de métodos cualitativos e investigación social.          |
| Andrea Lara Sánchez                 | Especialista de participación de la Jefatura de métodos cualitativos e investigación social.                 |

Fuente: elaboración propia.

## 2.2 Desarrollo de espacios participativos

La participación de los actores en los espacios participativos es completamente voluntaria. Para ello, se realiza un mapeo ampliado identificando a una diversidad de partes interesadas relevantes. La presencia de quienes han asistido responde a su decisión personal de involucrarse en el proceso y a una previa gestión de conflictos de intereses, la cual se describe a continuación.

Con este punto de partida, y en lo que respecta a la socialización y refinamiento de las preguntas de investigación de efectividad y seguridad, y las preguntas del

componente económico del posicionamiento terapéutico, se desarrolló un espacio deliberativo de forma virtual por medio de la plataforma de Microsoft Teams el día 11 de julio a las 6:00 p.m. Durante este espacio se socializó la propuesta de alcance, objetivos y preguntas en mención, promoviendo un diálogo abierto para recoger las percepciones, comentarios y recomendaciones por parte de los participantes. En la siguiente tabla se ilustra la trazabilidad de la asistencia:

**Tabla B-5. Participantes espacio deliberativo**

| No. | Organización que representa                         | Nombre                                  | Perfil                                                                                                                                                                                                               | Trazabilidad asistencia 1er espacio |
|-----|-----------------------------------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| 1   | Asociación Colombiana de Hematología y Oncología    | Herney Andrés García Perdomo            | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Magíster en epidemiología clínica. Doctor en educación. Doctor en ciencias biomédicas. Doctor en medicina clínica y salud pública. | Asiste                              |
| 2   | Sociedad Colombiana de Medicina Familiar            | Diego Alfonso Beltrán Martínez          | Médico y cirujano. Especialista en medicina familiar. Especialista en docencia universitaria. Magíster en epidemiología.                                                                                             | Asiste                              |
| 3   | Instituto Nacional de Cancerología                  | Germán Fabián Godoy Pérez               | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Especialista en educación para profesionales de la salud.                                                                          | Asiste                              |
| 4   | Ministerio de Salud y Protección Social             | Enrique Alejandro Robayo Duarte Químico | Químico farmacéutico. Especialista en dirección y gestión de proyectos. Magister (c) en políticas públicas.                                                                                                          | Asiste                              |
| 5   |                                                     | Inés María Galindo Henríquez            | Médica y cirujana. Especialista en epidemiología.                                                                                                                                                                    | Asiste                              |
| 6   |                                                     | Paula Andrea Romero Salcedo             | Economista. Magíster en economía.                                                                                                                                                                                    | Asiste                              |
| 7   | Instituto de Evaluación Tecnológica en Salud (IETS) | Johanna Echeverry                       | Epidemióloga de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                                                                                                                       | Asiste                              |
| 8   |                                                     | Jefferson Buendía                       | Epidemiólogo y coordinador de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                                                                                                         | Asiste                              |



| No. | Organización que representa | Nombre                   | Perfil                                                                                                 | Trazabilidad asistencia 1er espacio |
|-----|-----------------------------|--------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------|
| 9   |                             | Juan Camilo Martínez     | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.         | Asiste                              |
| 10  |                             | David Díaz-Báez          | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.         |                                     |
| 11  |                             | Lucas López Quiceno      | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.         | Asiste                              |
| 12  |                             | Grey Ceballos            | Economista de la Unidad de economía de la salud y analítica en salud.                                  | Asiste                              |
| 13  |                             | Angélica Ordóñez         | Economista de la Unidad de economía de la salud y analítica en salud.                                  | Asiste                              |
| 14  |                             | Sebastián Ortiz          | Economista de la Unidad de economía de la salud y analítica en salud.                                  | Asiste                              |
| 15  |                             | Gilberto Morales         | Analítico de la Unidad de economía de la salud y analítica en salud.                                   | Asiste                              |
| 16  |                             | Anamaría García          | Física y analítica de la de la Unidad de economía de la salud y analítica en salud.                    | Asiste                              |
| 17  |                             | María Camila Tavera      | Ingeniera biomédica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.  | Asiste                              |
| 18  |                             | Diana Segura             | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Asiste                              |
| 19  |                             | Suleidy Angarita Arévalo | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Asiste                              |
| 20  |                             | Andrea Lara Sánchez      | Especialista de participación de la Jefatura de métodos cualitativos e investigación social.           | Asiste                              |

Fuente: elaboración propia.

Posteriormente, para la socialización de la evidencia y la presentación de los resultados de costo efectividad y seguridad, se desarrolló un espacio deliberativo de forma virtual por medio de la plataforma de Microsoft Teams el día 14 de octubre a las 6:00 p.m. Durante este espacio se socializó la propuesta de alcance, objetivos y preguntas en mención, promoviendo un diálogo abierto para recoger las percepciones, comentarios y recomendaciones por parte de los participantes. En la siguiente tabla se ilustra la trazabilidad de la asistencia:

**Tabla B-6. Participantes espacio deliberativo**

| No.       | Organización que representa                                                           | Nombre                                  | Perfil                                                                                                                                                                                                               | Trazabilidad asistencia 2do espacio |
|-----------|---------------------------------------------------------------------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>1</b>  | Asociación Colombiana de Hematología y Oncología                                      | Herney Andrés García Perdomo            | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Magíster en epidemiología clínica. Doctor en educación. Doctor en ciencias biomédicas. Doctor en medicina clínica y salud pública. | Asiste                              |
| <b>2</b>  |                                                                                       | Ray Antonio Manneh Kopp                 | Médico y cirujano. Especialista en oncología clínica. Máster en oncología molecular.                                                                                                                                 | No asiste                           |
| <b>3</b>  | Asociación Colombiana de Hematología y Oncología / Instituto Nacional de Cancerología | Martín Ignacio Zapata Laguado           | Médico y cirujano. Especialista en medicina interna. Especialista en oncología clínica. Especialista en epidemiología clínica. Máster en oncología molecular.                                                        | Asiste                              |
| <b>4</b>  | Instituto Nacional de Cancerología                                                    | Germán Fabián Godoy Pérez               | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Especialista en educación para profesionales de la salud.                                                                          | Asiste                              |
| <b>5</b>  |                                                                                       | Humberto Varela Ramírez                 | Médico y cirujano. Especialista en medicina nuclear.                                                                                                                                                                 | No asiste                           |
| <b>6</b>  | Sociedad Colombiana de Medicina Familiar                                              | Diego Alfonso Beltrán Martínez          | Médico y cirujano. Especialista en medicina familiar. Especialista en docencia universitaria. Magíster en epidemiología.                                                                                             | Asiste                              |
| <b>7</b>  | Asociación Colombiana de Radioterapia                                                 | Ramiro David Bermúdez Iguarán           | Médico y cirujano. Especialista en oncología radioterápica. Magíster en radiocirugía y radioterapia. Magíster en epidemiología clínica.                                                                              | Asiste                              |
| <b>8</b>  |                                                                                       | Lina María Loaiza Salazar               | Médica y cirujana. Especialista en oncología radioterápica. Máster en cuidados paliativos. Actual presidente de la Sociedad.                                                                                         | Asiste                              |
| <b>9</b>  | Ministerio de Salud y Protección Social                                               | Enrique Alejandro Robayo Duarte Químico | Químico farmacéutico. Especialista en dirección y gestión de proyectos. Magister (c) en políticas públicas.                                                                                                          | Asiste                              |
| <b>10</b> |                                                                                       | Inés María Galindo Henríquez            | Médica y cirujana. Especialista en epidemiología.                                                                                                                                                                    | No asiste                           |

| No. | Organización que representa                         | Nombre                       | Perfil                                                                                                       | Trazabilidad asistencia 2do espacio |
|-----|-----------------------------------------------------|------------------------------|--------------------------------------------------------------------------------------------------------------|-------------------------------------|
| 11  |                                                     | David Eduardo Gómez Lizarazu | Economista. Magíster en estadística.                                                                         | No asiste                           |
| 12  |                                                     | Kelly Estrada Orozco         | Gerente técnica.                                                                                             | Asiste                              |
| 13  |                                                     | Johanna Echeverry            | Epidemióloga de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.               | Asiste                              |
| 14  |                                                     | Jefferson Buendía            | Epidemiólogo y coordinador de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Asiste                              |
| 15  |                                                     | Juan Camilo Martínez         | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.               | Asiste                              |
| 16  |                                                     | David Díaz-Báez              | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.               | Asiste                              |
| 17  |                                                     | Lucas López Quiceno          | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.               | Asiste                              |
| 18  | Instituto de Evaluación Tecnológica en Salud (IETS) | Grey Ceballos                | Economista de la Unidad de economía de la salud y analítica en salud.                                        | Asiste                              |
| 19  |                                                     | Angélica Ordóñez             | Economista de la Unidad de economía de la salud y analítica en salud.                                        | Asiste                              |
| 20  |                                                     | Sebastián Ortiz              | Economista de la Unidad de economía de la salud y analítica en salud.                                        | Asiste                              |
| 21  |                                                     | Gilberto Morales             | Analítico de la Unidad de economía de la salud y analítica en salud.                                         | Asiste                              |
| 22  |                                                     | Anamaría García              | Física y analítica de la de la Unidad de economía de la salud y analítica en salud.                          | Asiste                              |
| 23  |                                                     | María Camila Tavera          | Ingeniera biomédica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.        | Asiste                              |
| 24  |                                                     | Diana Segura                 | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.       | Asiste                              |
| 25  |                                                     | Suleidy Angarita Arévalo     | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.       | Asiste                              |
| 26  |                                                     | Fanny Emelina Torres García  | Profesional de apoyo a participación de la Jefatura de métodos cualitativos e investigación social.          | Asiste                              |

| No. | Organización que representa | Nombre              | Perfil                                                                                       | Trazabilidad asistencia 2do espacio |
|-----|-----------------------------|---------------------|----------------------------------------------------------------------------------------------|-------------------------------------|
| 27  |                             | Andrea Lara Sánchez | Especialista de participación de la Jefatura de métodos cualitativos e investigación social. | Asiste                              |

Fuente: elaboración propia.

Como compromiso de esta reunión, se envió a los expertos un resumen ejecutivo de los resultados y se envió un ejemplo de la votación, como preparación de la sesión final del posicionamiento. Esta última sesión se llevó a cabo el día 29 de octubre a las 6:00 p.m. de forma virtual por la plataforma de Microsoft Teams (la fecha y hora se coordinó conforme los resultados del sondeo de disponibilidad de agenda enviado a los expertos). A continuación, se ilustra la trazabilidad de la asistencia:

**Tabla B-7. Participantes espacio deliberativo**

| No. | Organización que representa                                                           | Nombre                        | Perfil                                                                                                                                                                                                               | Trazabilidad asistencia 2do espacio |
|-----|---------------------------------------------------------------------------------------|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| 1   | Asociación Colombiana de Hematología y Oncología                                      | Herney Andrés García Perdomo  | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Magíster en epidemiología clínica. Doctor en educación. Doctor en ciencias biomédicas. Doctor en medicina clínica y salud pública. | Asiste                              |
| 2   |                                                                                       | Ray Antonio Manneh Kopp       | Médico y cirujano. Especialista en oncología clínica. Máster en oncología molecular.                                                                                                                                 | Asiste                              |
| 3   | Asociación Colombiana de Hematología y Oncología / Instituto Nacional de Cancerología | Martín Ignacio Zapata Laguado | Médico y cirujano. Especialista en medicina interna. Especialista en oncología clínica. Especialista en epidemiología clínica. Máster en oncología molecular.                                                        | No asiste                           |
| 4   | Instituto Nacional de Cancerología                                                    | Germán Fabián Godoy Pérez     | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Especialista en educación para profesionales de la salud.                                                                          | Asiste                              |
| 5   |                                                                                       | Humberto Varela Ramírez       | Médico y cirujano. Especialista en medicina nuclear.                                                                                                                                                                 | Asiste                              |

| No. | Organización que representa                         | Nombre                                  | Perfil                                                                                                                                  | Trazabilidad asistencia 2do espacio |
|-----|-----------------------------------------------------|-----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| 6   |                                                     | Oscar Andrés Gamboa Garay               | Médico y cirujano. Especialista en oncología radioterápica. Especialista en estadística. Magíster en economía.                          | Asiste                              |
| 7   | Sociedad Colombiana de Medicina Familiar            | Diego Alfonso Beltrán Martínez          | Médico y cirujano. Especialista en medicina familiar. Especialista en docencia universitaria. Magíster en epidemiología.                | Asiste                              |
| 8   | Asociación Colombiana de Radioterapia               | Ramiro David Bermúdez Iguarán           | Médico y cirujano. Especialista en oncología radioterápica. Magíster en radiocirugía y radioterapia. Magíster en epidemiología clínica. | Asiste                              |
| 9   |                                                     | Lina María Loaiza Salazar               | Médica y cirujana. Especialista en oncología radioterápica. Máster en cuidados paliativos. Actual presidente de la Sociedad.            | Asiste                              |
| 10  | Ministerio de Salud y Protección Social             | Enrique Alejandro Robayo Duarte Químico | Químico farmacéutico. Especialista en dirección y gestión de proyectos. Magister (c) en políticas públicas.                             | No asiste                           |
| 11  |                                                     | Inés María Galindo Henríquez            | Médica y cirujana. Especialista en epidemiología.                                                                                       | No asiste                           |
| 12  |                                                     | David Eduardo Gómez Lizarazu            | Economista. Magíster en estadística.                                                                                                    | No asiste                           |
| 13  | Instituto de Evaluación Tecnológica en Salud (IETS) | Kelly Estrada Orozco                    | Gerente técnica.                                                                                                                        | Asiste                              |
| 14  |                                                     | Johanna Echeverry                       | Epidemióloga de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                                          | Asiste                              |
| 15  |                                                     | Jefferson Buendía                       | Epidemiólogo y coordinador de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                            | Asiste                              |
| 16  |                                                     | Juan Camilo Martínez                    | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                                          | Asiste                              |
| 17  |                                                     | David Díaz-Báez                         | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                                          | Asiste                              |
| 18  |                                                     | Lucas López Quiceno                     | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                                          | Asiste                              |

| No. | Organización que representa | Nombre                      | Perfil                                                                                                 | Trazabilidad asistencia 2do espacio |
|-----|-----------------------------|-----------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------|
| 19  |                             | Grey Ceballos               | Economista de la Unidad de economía de la salud y analítica en salud.                                  | Asiste                              |
| 20  |                             | Angélica Ordóñez            | Economista de la Unidad de economía de la salud y analítica en salud.                                  | Asiste                              |
| 21  |                             | Sebastián Ortiz             | Economista de la Unidad de economía de la salud y analítica en salud.                                  | Asiste                              |
| 22  |                             | Gilberto Morales            | Analítico de la Unidad de economía de la salud y analítica en salud.                                   | Asiste                              |
| 23  |                             | Anamaría García             | Física y analítica de la de la Unidad de economía de la salud y analítica en salud.                    | Asiste                              |
| 24  |                             | María Camila Tavera         | Ingeniera biomédica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.  | Asiste                              |
| 25  |                             | Diana Segura                | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Asiste                              |
| 26  |                             | Suleidy Angarita Arévalo    | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Asiste                              |
| 27  |                             | Fanny Emelina Torres García | Profesional de apoyo a participación de la Jefatura de métodos cualitativos e investigación social.    | Asiste                              |
| 28  |                             | Andrea Lara Sánchez         | Especialista de participación de la Jefatura de métodos cualitativos e investigación social.           | Asiste                              |

Fuente: elaboración propia.

Por requerimiento de los expertos, la pregunta 4 requirió una revisión y ajuste, por lo que fue enviada para votación asincrónica a los expertos participantes.

## 2.3 Gestión de los conflictos de intereses

Se parte de entender los conflictos de intereses (CDI) como aquellas “*posibles situaciones de orden moral, intelectual y económico que pueden impedirle a una persona actuar en forma objetiva e independiente, ya sea porque le resulte particularmente conveniente, le sea personalmente beneficioso o porque sus familiares en los grados indicados en la ley se vean igualmente beneficiados*” (6). En otras palabras, los conflictos de intereses son las tensiones que existen

cuando los intereses privados pueden llegar a prevalecer sobre los intereses generales, colectivos o públicos (7).

En el IETS se ha establecido la política de transparencia mediante la cual se busca gestionar de forma adecuada los potenciales conflictos de intereses, asegurando la legitimidad y la transparencia de todos los procesos que el IETS tiene a su cargo, especialmente garantizando que quienes participen en los procesos no tengan intereses que puedan afectar su objetividad o incidir en las recomendaciones a favor de sus intereses personales (8).

Sin embargo, en el marco del posicionamiento terapéutico de cáncer de próstata, se aplicó un ajuste metodológico en el proceso de involucramiento de expertos y, por tanto, en la gestión de los conflictos de intereses. Esto, debido a la necesidad de involucrar expertos que, a pesar de sus potenciales conflictos de intereses, son líderes reconocidos en el abordaje del cáncer de próstata (tienen una experticia crítica para los análisis desarrollados en el posicionamiento) y que, además, contaban con la disponibilidad para participar en el proceso.

Así, se definieron estrategias específicas para reducir el riesgo de materialización de sus potenciales intereses como el establecimiento de ponderaciones (ver sección de votación del documento) y el contar con la participación del 51% de asistentes sin conflictos de intereses directos con el tema (9). Con este balance, se busco gestionar de la manera más adecuada los potenciales conflictos de forma que participaran los expertos en el tema, pero sin afectar su objetividad.

Con estas precisiones, el proceso de identificación y gestión de los CDI potenciales inició con la declaración de estos por parte de los participantes. Para ello, el IETS dispone de un formato electrónico cuyo enlace se puede ver aquí: <http://herramientas.iets.org.co/declaracion/home.aspx>. Una vez los participantes diligenciaron el formato de declaración de CDI, la información entregada se analizó por parte del Comité de gestión de los conflictos de intereses con el fin de identificar, tipificar y gestionar los potenciales conflictos. Esta valoración se repitió cuando se hizo la consulta, por parte del Ministerio de Salud y Protección Social, al Registro de transferencias de valor entre actores del sector salud (RTVSS).

Para la adecuada gestión de los conflictos, como ya se mencionó, la deliberación del comité parte del reconocimiento la inevitable tensión entre procurar el derecho a la participación y, al mismo tiempo, generar condiciones adecuadas

que no les resten legitimidad, validez y confiabilidad a la emisión de recomendaciones que se generan desde el IETS (8).

También se toman en cuenta los hechos con vigencia de dos años hacia atrás del momento en el que se hace la declaración, así como las características de los procesos o proyectos en los que las personas participarán o ejercerán sus funciones. Valorando caso a caso, se tipifican los conflictos de intereses (si son financieros, no financieros, personales u organizacionales), y se valora la experticia en función del tema utilizando una matriz que facilita el análisis y la ponderación de la experticia y del conflicto potencial (7).

Para los casos en los que la información consignada en los formatos no es suficiente, se solicita la aclaración respectiva por correo electrónico. Las respuestas enviadas por los actores también son tenidas en cuenta como elementos adicionales de análisis.

Con estos insumos de análisis (la experiencia y trayectoria profesional, la declaración de los potenciales CDI, las aclaraciones adicionales y, en este caso del posicionamiento, la consulta hecha por el Ministerio al RTVSS), el comité definió el alcance de la participación de los actores de acuerdo con los niveles establecidos en la Política de transparencia, como se muestra en la siguiente tabla:

**Tabla B-8. Categorías de participación**

| Alcance de la participación | Definición                                                                                                                                                                                                                                                                                                      | Implicación                                                                                                                                                                                                                                                                      |
|-----------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Participación</b>        | Identifica el conflicto como inexistente. Esta condición ocurre cuando la persona no declara ningún interés en particular o cuando se declara algún interés que no guarda relación específica con el tema, proyecto o proceso.                                                                                  | La persona puede participar en todos los procesos y pasos sin limitaciones.                                                                                                                                                                                                      |
| <b>Limitación parcial</b>   | Identifica el conflicto como probable. Esta condición ocurre cuando la persona declara un interés particular que, a consideración del comité, podría afectar la independencia y objetividad de la persona de alguna manera, pero que no le impide completamente su participación en algunas etapas del proceso. | Se limita la participación del individuo en el proceso o procesos relacionados con el interés (específico o no específico) declarado y considerado potencialmente conflictivo. Así, su participación solo se dará en aquellos ámbitos en los que el conflicto no se materialice. |



| Alcance de la participación | Definición                                                                                                                                                               | Implicación                                                                                                                                                                                                     |
|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Exclusión</b>            | Identifica el conflicto como confirmado. Esta situación ocurre cuando el comité identifica un claro conflicto de los intereses de la persona con el proceso en cuestión. | Se considera que, dada la importancia de los intereses declarados y su relación con el tema de interés, el individuo no debe participar ya que pondría en riesgo la validez del y/o la confianza en el proceso. |

Fuente: Elaborado a partir de Política de transparencia (6).

Para los casos en los que la participación es limitada o no puede darse, se delibera sobre los posibles cursos de acción que buscan alcanzar un equilibrio reflexivo (7), lo que quiere decir que se pretende optimizar la experticia y disminuir el riesgo de materialización de los conflictos de intereses, generando recomendaciones de acción.

Con estas consideraciones, se presenta a continuación la síntesis de los resultados del análisis y deliberación del comité de gestión de CDI respecto a los expertos participantes:

**Tabla B-9. Matriz síntesis de declaración y análisis de conflictos de interés**

| Nombre                       | Rol                             | Intereses declarados                                                                                                                             | Experticia soportada para el producto                                                                                                                                                       | Tipo de conflicto de interés identificado        | Resultado deliberación Comité de gestión de conflictos de Interés                                                                                                                                             |
|------------------------------|---------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Herney Andrés García Perdomo | Experto del grupo desarrollador | Menciona que ha participado en eventos sobre prevención y detección temprana de cáncer de próstata, con patrocinio de la industria farmacéutica. | Médico y cirujano. Especialista en urología. Especialista en urología oncológica. Magíster en epidemiología clínica. Doctor en educación. Doctor en ciencias biomédicas. Doctor en medicina | Conflicto de interés financiero y no específico. | Considerando que el posicionamiento terapéutico está relacionado con el tratamiento, más no con la prevención, el riesgo del potencial conflicto es bajo. Por tanto, se le da aval de participación completa. |

| Nombre                        | Rol                             | Intereses declarados                                                                                                              | Experticia soportada para el producto                                                                                                                         | Tipo de conflicto de interés identificado     | Resultado deliberación Comité de gestión de conflictos de Interés                                                                                                                                                                                                                                                |
|-------------------------------|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                               |                                 |                                                                                                                                   | clínica y salud pública.                                                                                                                                      |                                               |                                                                                                                                                                                                                                                                                                                  |
| Ray Antonio Manneh Kopp       | Experto del grupo desarrollador | Menciona que ha participado en eventos y que ha sido conferencista para varias industrias farmacéuticas sobre cáncer de próstata. | Médico y cirujano. Especialista en oncología clínica. Máster en oncología molecular.                                                                          | Conflicto de interés financiero y específico. | En un primer momento, el comité decidió que no podía participar en el proceso. Sin embargo, dada la necesidad de contar con su experiencia en el proceso, el comité revaloró su participación, considerando los ajustes metodológicos para asegurar la no materialización del riesgo de conflictos de intereses. |
| Martín Ignacio Zapata Laguado | Experto del grupo desarrollador | Menciona que ha participado en eventos y que ha sido conferencista para varias industrias farmacéuticas sobre cáncer de próstata. | Médico y cirujano. Especialista en medicina interna. Especialista en oncología clínica. Especialista en epidemiología clínica. Máster en oncología molecular. | Conflicto de interés financiero y específico. | En un primer momento, el comité decidió que no podía participar en el proceso. Sin embargo, dada la necesidad de contar con su experiencia en el proceso, el comité revaloró su participación, considerando los ajustes metodológicos para asegurar la                                                           |

| Nombre                         | Rol                             | Intereses declarados                                                                     | Experticia soportada para el producto                                                                                                           | Tipo de conflicto de interés identificado        | Resultado deliberación Comité de gestión de conflictos de Interés                                                                              |
|--------------------------------|---------------------------------|------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
|                                |                                 |                                                                                          |                                                                                                                                                 |                                                  | no materialización del riesgo de conflictos de intereses.                                                                                      |
| Diego Alfonso Beltrán Martínez | Experto del grupo desarrollador | No declara intereses relacionados con el tema en la herramienta de declaración del IETS. | Médico y cirujano. Especialista en medicina familiar. Especialista en docencia universitaria. Magíster en epidemiología.                        | Ninguno                                          | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa.                                            |
| Germán Fabián Godoy Pérez      | Experto del grupo desarrollador | Declara la participación en un evento de cáncer de próstata en el INC.                   | Médico y cirujano. Especialista en urología. Sub-especialista en urología oncológica. Especialista en educación para profesionales de la salud. | Conflicto de interés financiero y no específico. | Conforme su aclaración, el comité considera que el riesgo del potencial conflicto es bajo. Por tanto, se le da aval de participación completa. |
| Humberto Varela Ramírez        | Experto del grupo desarrollador | No declara intereses relacionados con el tema en la herramienta de declaración del IETS. | Médico y cirujano. Especialista en medicina nuclear.                                                                                            | Ninguno                                          | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa.                                            |
| Ramiro David                   | Experto del grupo desarrollador | No declara intereses relacionados                                                        | Médico y cirujano. Especialista                                                                                                                 | Ninguno                                          | Al no tener conflictos de intereses                                                                                                            |

| Nombre                    | Rol                                        | Intereses declarados                                                                                      | Experticia soportada para el producto                                                                                        | Tipo de conflicto de interés identificado        | Resultado deliberación Comité de gestión de conflictos de Interés                                                                              |
|---------------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| Bermúdez Iguarán          |                                            | con el tema en la herramienta de declaración del IETS.                                                    | en oncología radioterápica. Magíster en radiocirugía y radioterapia. Magíster en epidemiología clínica.                      |                                                  | relacionados con el tema, tiene aval de participación completa.                                                                                |
| Lina María Loaiza Salazar | Experta del grupo desarrollador            | Menciona participar como asistente y conferencista en un evento de la sociedad científica que representa. | Médica y cirujana. Especialista en oncología radioterápica. Máster en cuidados paliativos. Actual presidente de la Sociedad. | Conflicto de interés financiero y no específico. | Conforme su aclaración, el comité considera que el riesgo del potencial conflicto es bajo. Por tanto, se le da aval de participación completa. |
| Oscar Andrés Gamboa Garay | Experto participante                       | No declara intereses relacionados con el tema.                                                            | Médica y cirujana. Especialista en oncología radioterápica. Especialista en estadística. Magíster en economía.               | Ninguno                                          | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa.                                            |
| Johanna Echeverry         | Experta metodóloga del grupo desarrollador | No declara intereses relacionados con el tema.                                                            | Epidemióloga de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.                               | Ninguno                                          | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa.                                            |
| Jefferson Buendía         | Experto metodólogo del grupo desarrollador | No declara intereses relacionados con el tema.                                                            | Epidemiólogo y coordinador de la Unidad de síntesis de                                                                       | Ninguno                                          | Al no tener conflictos de intereses relacionados con                                                                                           |

| Nombre               | Rol                                        | Intereses declarados                           | Experticia soportada para el producto                                                          | Tipo de conflicto de interés identificado | Resultado deliberación Comité de gestión de conflictos de Interés                                   |
|----------------------|--------------------------------------------|------------------------------------------------|------------------------------------------------------------------------------------------------|-------------------------------------------|-----------------------------------------------------------------------------------------------------|
|                      |                                            |                                                | la evidencia y gestión de las tecnologías sanitarias.                                          |                                           | el tema, tiene aval de participación completa.                                                      |
| Juan Camilo Martínez | Experto metodólogo del grupo desarrollador | No declara intereses relacionados con el tema. | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| Lucas López Quiceno  | Experto metodólogo del grupo desarrollador | No declara intereses relacionados con el tema. | Epidemiólogo de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| Grey Ceballos        | Experta metodóloga del grupo desarrollador | No declara intereses relacionados con el tema. | Economista de la Unidad de economía de la salud y analítica en salud.                          | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| Angélica Ordóñez     | Experta metodóloga del grupo desarrollador | No declara intereses relacionados con el tema. | Economista de la Unidad de economía de la salud y analítica en salud.                          | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| Sebastián Ortiz      | Experto metodólogo del grupo desarrollador | No declara intereses relacionados con el tema. | Economista de la Unidad de economía de la salud y                                              | Ninguno                                   | Al no tener conflictos de intereses relacionados con                                                |

| Nombre                   | Rol                                        | Intereses declarados                           | Experticia soportada para el producto                                                                  | Tipo de conflicto de interés identificado | Resultado deliberación Comité de gestión de conflictos de Interés                                   |
|--------------------------|--------------------------------------------|------------------------------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------------|-----------------------------------------------------------------------------------------------------|
|                          |                                            |                                                | analítica en salud.                                                                                    |                                           | el tema, tiene aval de participación completa.                                                      |
| Gilberto Morales         | Experto metodólogo del grupo desarrollador | No declara intereses relacionados con el tema. | Analítico de la Unidad de economía de la salud y analítica en salud.                                   | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| Anamaría García          | Experta metodóloga del grupo desarrollador | No declara intereses relacionados con el tema. | Física y analítica de la de la Unidad de economía de la salud y analítica en salud.                    | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| María Camila Tavera      | Experta metodóloga del grupo desarrollador | No declara intereses relacionados con el tema. | Ingeniera biomédica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias.  | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| Diana Segura             | Experta metodóloga del grupo desarrollador | No declara intereses relacionados con el tema. | Química farmacéutica de la Unidad de síntesis de la evidencia y gestión de las tecnologías sanitarias. | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |
| Suleidy Angarita Arévalo | Experta metodóloga                         | No declara intereses                           | Química farmacéutica de la Unidad                                                                      | Ninguno                                   | Al no tener conflictos de intereses                                                                 |

| Nombre              | Rol                          | Intereses declarados                           | Experticia soportada para el producto                                     | Tipo de conflicto de interés identificado | Resultado deliberación Comité de gestión de conflictos de Interés                                   |
|---------------------|------------------------------|------------------------------------------------|---------------------------------------------------------------------------|-------------------------------------------|-----------------------------------------------------------------------------------------------------|
|                     | del grupo desarrollador      | relacionados con el tema.                      | de síntesis de la evidencia y gestión de las tecnologías sanitarias.      |                                           | relacionados con el tema, tiene aval de participación completa.                                     |
| Andrea Lara Sánchez | Profesional de participación | No declara intereses relacionados con el tema. | Politóloga de la Jefatura de Métodos cualitativos e investigación social. | Ninguno                                   | Al no tener conflictos de intereses relacionados con el tema, tiene aval de participación completa. |

Fuente: elaboración propia.

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## Anexo B.2 Informe técnico de síntesis de las mesas de socialización

### Primera sesión de socialización de preguntas y alcance

El 11 de julio de 2025, se organizó la primera mesa de socialización y de refinamiento de preguntas preliminares del actual posicionamiento terapéutico para el tratamiento farmacológico del cáncer de próstata a través de la plataforma Microsoft Teams, con la participación de expertos especialistas clínicos y representantes del Ministerio de Salud y Protección Social. A continuación, se muestra la trazabilidad de la asistencia:

Los asistentes al primer espacio de socialización se detallan en el **Anexo B1**, *Error! No se encuentra el origen de la referencia..*

La sesión comenzó a las 6:00 PM, con una presentación introductoria por parte del grupo desarrollador que cubrió los siguientes aspectos principales:

- **Definición de posicionamiento terapéutico**  
Se explicó a los asistentes que es un posicionamiento terapéutico, qué busca, a quién va dirigido y su impacto en el sistema de salud.
- **Etapas y metodologías del posicionamiento terapéutico**  
Se explicaron las etapas que se desarrollan dentro un posicionamiento terapéutico y los actores involucrados en cada una de ellas como son:
  - Definición del alcance, etapa que incluye la búsqueda de la información sobre la condición de salud para poder identificar dentro del espectro de la enfermedad cuales son los grupos poblacionales que deban ser incluidos en el PT. Además, en esta fase se incluye la búsqueda de evaluaciones económicas e indicaciones INVIMA de los medicamentos empleados en el tratamiento del cáncer de próstata. Todo con el propósito de elaborar la propuesta de las preguntas PICO que guiaran la evaluación de efectividad y seguridad, así como la evaluación económica.
  - Búsqueda sistemática y extracción de la información, etapa en la cual se desarrollan las búsquedas de efectividad, de seguridad, las

estimaciones de costos, la verificación de la dosificación de los distintos esquemas terapéuticos, así como las probabilidades de efectividad y eventos adversos que alimentarán el modelo con el cual se realizará la evaluación económica.

- Evaluación de efectividad y seguridad, fase en la cual se sintetiza la evidencia recuperada, se realizan los análisis estadísticos y económicos requeridos que darán repuesta a las preguntas planteadas para poder obtener el ordenamiento de las moléculas que se van a posicionar.
- Etapa de posicionamiento, donde se recoge la precepción desde la óptica del prescriptor mediante un proceso de votación para luego obtener el ordenamiento de las tecnologías y proceder a la elaboración final del documento.

Se explicó el proceso detallado de cómo se desarrolla la evaluación de efectividad y seguridad, así como el proceso que se lleva a cabo para la evaluación económica.

- Alcance: Se presentó el alcance que incluye evaluar alternativas farmacológicas para el tratamiento del cáncer de próstata de acuerdo con las etapas clínicas y la sensibilidad a hormonas, con el objetivo de establecer una jerarquización de tecnologías disponibles en Colombia. Planteando las siguiente alternativas y escenarios clínicos:
  - Alternativas Farmacológicas: El posicionamiento terapéutico evaluará alternativas farmacológicas, incluyendo combinaciones de inmunoterapia para el tratamiento del cáncer de próstata en pacientes adultos, considerando la etapa clínica y la sensibilidad a hormonas.
  - Escenarios Clínicos: Se evaluarán cuatro escenarios clínicos específicos: cáncer de próstata localizado o de alto riesgo, localmente avanzado o regional, no metastásico resistente a castración, y metastásico hormono sensible y resistente a la castración.
- Objetivo: Se presentó el objetivo que pretende establecer una jerarquización de tecnologías disponibles en Colombia para el tratamiento del cáncer de próstata en adultos, de acuerdo con los diferentes estadios clínicos y la sensibilidad a hormonas.

- Preguntas de evaluación de efectividad y seguridad: Se presentaron las 4 preguntas preliminarmente planteadas que provienen de un ejercicio derivado de la búsqueda y revisión de datos en GPC y estudios relacionados con cáncer de próstata y de un proceso de refinamiento preliminar con referentes técnicos del MSPS y de un experto clínico que acompaña al grupo desarrollador. En cada pregunta se dio lectura del I escenario clínico (población), a las intervenciones, comparadores, desenlaces y tipos de estudios previstos para cada una de las preguntas.
- Preguntas de evaluación de efectividad y seguridad: se presentaron 4 preguntas aclarando que el componente de población, intervenciones y comparadores es exactamente igual a las preguntas de efectividad y seguridad u se presenta para cada una de ellas el desenlace económico que se evaluará (AVAC), el horizonte temporal y la perspectiva de tercer pagador que se empleará.

Posterior a la presentación se abrió espacio para la discusión y comentarios por parte de profesionales médicos con experiencia en el manejo de la condición de salud asistentes al espacio.

En general los expertos estuvieron de acuerdo con las preguntas presentadas aclarando que eran metodológicamente correctas en su formulación y se empezaron a revisar una a una las preguntas de efectividad y seguridad, aclarando que cualquier ajuste que se realizará en ellas se realizaría de igual manera en las preguntas de la evaluación económica.

Se discutieron y ajustaron aspectos como:

- Dosificación de la prednisona/prednisolona: se realizó ajuste cuando acompaña a la abiraterona y al cabazitaxel, estableciendo una dosis de 5 mg en (pregunta 3) y de 5 mg cada 12 horas para pacientes con cáncer de próstata metastásico resistente a castración (pregunta 4).
- Con respecto a los análogos y antagonistas: se aclaró que se debe mantener el mismo análogo o antagonista de GnRH que el paciente venía utilizando en la fase hormono sensible, y se discutió la continuidad del tratamiento con estos medicamentos.

- Con relación a la clasificación TPA se aclara en las preguntas PICO que TPA se refiere a bloqueo de GnRH, incluyendo tanto análogos como antagonistas.
- Con respecto a eliminación de grupos y/o medicamentos: Se eliminó un subgrupo de combinaciones de terapias (dupletas que incluyen combinación de docetaxel con antiandrógenos) que no se emplean de manera simultánea en la fase del cáncer de próstata metastásico resistente a castración (pregunta 4), basándose en la práctica clínica. Con respecto a darolutamina y docetaxel se aclara que no pueden quedar dentro del posicionamiento de la pregunta 3 y 4 dado que las indicaciones de uso otorgadas por el Invima, no lo permite.

## **Anexo C. Calificación de los desenlaces**

Durante la fase de socialización que se realizó el 11 de julio de 2025, se discutieron con los expertos temáticos los posibles desenlaces a medir para cada pregunta PICO con el objetivo de buscar, sintetizar y analizar la evidencia para la comparación de las tecnologías a posicionar.

Se construyó un listado preliminar de desenlaces, a partir de búsquedas de literatura (ECA y GPC). Este listado de desenlaces fue propuesto sin conocer a priori la dirección, la significancia estadística y la magnitud de los efectos, así como la disponibilidad de evidencia científica y su calidad metodológica. El listado preliminar fue revisado y complementado por los expertos temáticos del grupo desarrollador.

Posteriormente, se hizo la discusión de la importancia de los desenlaces, proceso realizado por los expertos clínicos, quienes valoraron cada desenlace de forma individual e independiente, para la calificación de los desenlaces se siguieron las recomendaciones del manual GRADE y la Guía metodológica para la elaboración de guías de práctica clínica (1,2) (Tabla C 1).

**Tabla C-1. Escala para la valoración de la importancia de los desenlaces de acuerdo con el sistema GRADE**

| 1                                                                                           | 2 | 3 | 4                                                                                             | 5 | 6 | 7                                                                         | 8 | 9 |
|---------------------------------------------------------------------------------------------|---|---|-----------------------------------------------------------------------------------------------|---|---|---------------------------------------------------------------------------|---|---|
| De importancia limitada para la toma de decisiones (no incluidos en el perfil de evidencia) |   |   | Importantes, mas no críticos para la toma de decisiones (incluidos en el perfil de evidencia) |   |   | Críticos para la toma de decisiones (incluidos en el perfil de evidencia) |   |   |

Fuente: elaboración propia.

Producto de este ejercicio, se incluyeron en la pregunta de investigación aquellos desenlaces clasificados como críticos y los desenlaces importantes más no críticos para la toma de decisiones; los desenlaces identificados como no importantes para la toma de decisiones no fueron considerados para el proceso de revisión.

A continuación, se presenta la categorización realizada por los integrantes y la clasificación final de cada desenlace:

**Tabla C-2. Resultado de la clasificación de los desenlaces**

| Desenlace                                                     | Relevancia |
|---------------------------------------------------------------|------------|
| 1. Supervivencia global                                       | Critico    |
| 2. Supervivencia libre de progresión                          | Importante |
| 3. Supervivencia libre de metástasis                          | Importante |
| 4. Supervivencia libre de progresión bioquímica basada en PSA | Importante |
| 5. Tasa de respuesta objetiva                                 | Importante |
| 6. Tasa de respuesta del PSA                                  | Importante |
| 7. Calidad de vida relacionada con la salud                   | Importante |
| 8. Eventos adversos totales                                   | Importante |
| 9. Eventos adversos graves                                    | Importante |
| 10. Eventos adversos relacionados con el tratamiento          | Importante |

## Anexo D. Estrategias de búsqueda para la evaluación de efectividad y seguridad

### Anexo D.1 Revisiones sistemáticas de la literatura y estudios primarios (Ensayos Clínicos)

**Tabla D-1. Estrategia de búsqueda MEDLINE**

| Característica             | Reporte                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
|----------------------------|------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Tipo de búsqueda           | Nueva                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Bases de datos             | Medline                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Plataforma                 | PubMed                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Fecha de búsqueda          | 26/06/2025                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Rango de fecha de búsqueda | Ninguna                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Restricciones de lenguaje  | Ninguna                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Otros límites              | Revisiones sistemáticas y metaanálisis<br>Ensayos clínicos |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Estrategia de búsqueda     | #                                                          | Búsqueda                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Resultados |
|                            | 1                                                          | (leuporeline[Title/Abstract]) OR<br>((((((((((((((((((((LHRH agonist[Title/Abstract])<br>OR (Goserelin[Title/Abstract])) OR<br>(Leuprolide[Title/Abstract])) OR<br>(Triptorelin[Title/Abstract])) OR (GnRH<br>antagonist[Title/Abstract])) OR<br>(Degarelix[Title/Abstract])) OR<br>(abiraterone[Title/Abstract])) OR<br>(antiandrogen[Title/Abstract])) OR<br>(bicalutamide[Title/Abstract])) OR<br>(flutamide[Title/Abstract])) OR (androgen<br>deprivation[Title/Abstract])) OR<br>(Enzalutamide[Title/Abstract])) OR<br>(apalutamide[Title/Abstract])) OR<br>(Darolutamide[Title/Abstract])) OR<br>(Docetaxel[Title/Abstract])) OR<br>(Cabazitaxel[Title/Abstract])) OR<br>(taxanes[Title/Abstract])) OR<br>(Ciproterone[Title/Abstract])) OR | 71331      |

|  |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |        |
|--|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
|  |   | (Olaparib[Title/Abstract])) OR<br>(Radium[Title/Abstract])) OR<br>(Lutetium[Title/Abstract])) OR<br>(Diethylstilbestrol[Title/Abstract])) OR (Ra-<br>223[Title/Abstract])) OR (Lu-177[Title/Abstract]))<br>OR "Mitoxantrone"[Title/Abstract]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |
|  | 2 | (((((Goserelin[Mesh]) OR<br>("Leuprolide"[Mesh])) OR ("Triptorelin<br>Pamoate"[Mesh])) OR ("Gonadotropin-Releasing<br>Hormone"[Mesh])) OR ("acetyl-2-naphthylalanyl-3-<br>chlorophenylalanyl-1-oxohexadecyl-seryl-4-<br>aminophenylalanyl(hydroxyrotyl)-4-<br>aminophenylalanyl(carbamoyl)-leucyl-ILys-prolyl-<br>alaninamide" [Supplementary Concept])) OR<br>("Abiraterone Acetate"[Mesh] OR "abiraterone"<br>[Supplementary Concept])) OR ("Androgen<br>Antagonists"[Mesh])) OR ("bicalutamide"<br>[Supplementary Concept])) OR<br>("Flutamide"[Mesh])) OR ("enzalutamide"<br>[Supplementary Concept])) OR ("apalutamide"<br>[Supplementary Concept])) OR ("darolutamide"<br>[Supplementary Concept])) OR (Taxoids[Mesh])) OR<br>("Docetaxel"[Mesh])) OR ("cabazitaxel"<br>[Supplementary Concept])) OR ("olaparib"<br>[Supplementary Concept])) OR ("Radium"[Mesh] OR<br>"Radium-223" [Supplementary Concept] OR "radium<br>Ra 223 dichloride" [Supplementary Concept])) OR<br>("Lutetium-177" [Supplementary Concept])) OR<br>("Diethylstilbestrol"[Mesh])) OR<br>(Radiotherapy[Mesh] OR "radiotherapy"<br>[Subheading]) OR "Mitoxantrone"[MeSH Terms] | 434949 |
|  | 3 | (((((L02AE03) OR (L02AE51)) OR<br>(L02AE02)) OR (L02AE04)) OR (L02BX02)) OR<br>(L01XK52)) OR (L02BX03)) OR (L02BX53)) OR<br>(L02BB03)) OR (L02BB01)) OR (L02BB02)) OR<br>(L02BB04)) OR (L02BB05)) OR (L02BB06)) OR<br>(L01CD02)) OR (G03HA01)) OR (L01CD04)) OR<br>(L01XK01)) OR (L02AA01) - Schema: all - Schema:<br>all                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0      |
|  | 4 | (((((L02AE03) OR (L02AE51)) OR<br>(L02AE02)) OR (L02AE04)) OR (L02BX02)) OR<br>(L01XK52)) OR (L02BX03)) OR (L02BX53)) OR<br>(L02BB03)) OR (L02BB01)) OR (L02BB02)) OR<br>(L02BB04)) OR (L02BB05)) OR (L02BB06)) OR<br>(L01CD02)) OR (G03HA01)) OR (L01CD04)) OR<br>(L01XK01)) OR (L02AA01) - Schema: all                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0      |
|  | 5 | ((luteinizing Hormone Releasing Hormone<br>Agonist[Title/Abstract]) OR (Gonadotropin Releasing<br>Hormone Agonist[Title/Abstract])) OR (Luteinizing<br>Hormone Releasing Hormone<br>Antagonist[Title/Abstract])                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 2943   |
|  | 6 | (((((Zoladex[Title/Abstract]) OR<br>(Eligard[Title/Abstract])) OR<br>(Lupron[Title/Abstract])) OR<br>(Viadur[Title/Abstract])) OR<br>(Trelstar[Title/Abstract])) OR<br>(Firmagon[Title/Abstract])) OR<br>(Abirtega[Title/Abstract])) OR<br>(Zytiga[Title/Abstract])) OR<br>(Orgovyx[Title/Abstract])) OR<br>(Plenaxis[Title/Abstract])) OR                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1847   |

|                                        |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |         |
|----------------------------------------|----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
|                                        |    | (Casodex[Title/Abstract])) OR<br>(Eulexin[Title/Abstract])) OR<br>(Xtandi[Title/Abstract])) OR<br>(Erleada[Title/Abstract])) OR<br>(Nubeqa[Title/Abstract])) OR<br>(Beizray[Title/Abstract])) OR<br>(Docivvyx[Title/Abstract])) OR<br>(Androcur[Title/Abstract])) OR<br>(Jevtana[Title/Abstract])) OR<br>(Lynparza[Title/Abstract])) OR<br>(Apstil[Title/Abstract])) OR<br>(Boestrol[Title/Abstract])) OR<br>(Destibenol[Title/Abstract])) OR<br>(Distibene[Title/Abstract])) OR<br>(Honvol[Title/Abstract])) OR<br>(Stilbestrol[Title/Abstract])) |         |
|                                        | 7  | #1 OR #2 OR #5 OR #6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 462388  |
|                                        | 8  | "prostatic neoplasms"[MeSH Terms] OR<br>("prostatic"[All Fields] AND "neoplasms"[All Fields])<br>OR "prostatic neoplasms"[All Fields] OR<br>("prostate"[All Fields] AND "cancer"[All Fields]) OR<br>"prostate cancer"[All Fields]                                                                                                                                                                                                                                                                                                                  | 228331  |
|                                        | 9  | ("prostatic neoplasms"[MeSH Terms] OR "prostatic<br>neoplasms"[Title/Abstract] OR "neoplasm*<br>prostatic"[Title/Abstract] OR "prostatic<br>neoplasm*"[Title/Abstract] OR "neoplasm*<br>prostate"[Title/Abstract] OR "prostate<br>cancer"[Title/Abstract] OR "prostatic<br>cancer*"[Title/Abstract] OR "cancer of<br>prostate"[Title/Abstract])                                                                                                                                                                                                    | 203909  |
|                                        | 10 | #8 OR #9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 228680  |
|                                        | 11 | #7 AND #10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 49681   |
|                                        | 12 | randomized controlled trial[Publication Type] OR<br>randomized[Title/Abstract] OR<br>placebo[Title/Abstract]                                                                                                                                                                                                                                                                                                                                                                                                                                       | 1131061 |
|                                        | 13 | MEDLINE[Title/Abstract] OR<br>(systematic[Title/Abstract] AND<br>review[Title/Abstract]) OR meta-analysis[Publication<br>Type]                                                                                                                                                                                                                                                                                                                                                                                                                     | 585634  |
|                                        | 14 | #12 OR #13                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 1588732 |
|                                        | 15 | #11 AND #14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 6006    |
| Número de referencias<br>identificadas |    | <b>6006</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |

Fuente: elaboración propia.



**Tabla D-2. Estrategia de búsqueda EMBASE**

| Característica             | Reporte    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
|----------------------------|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Tipo de búsqueda           | Nueva      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| Bases de datos             | Embase     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| Plataforma                 | Embase     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| Fecha de búsqueda          | 26/06/2025 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| Rango de fecha de búsqueda | Ninguna    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| Restricciones de lenguaje  | Ninguna    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| Otros límites              | Ninguna    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| Estrategia de búsqueda     | #          | Búsqueda                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Resultados |
|                            | 1          | 'lhrh agonist':ti,ab,kw OR 'goserelin':ti,ab,kw<br>OR 'leuprolide':ti,ab,kw OR<br>'triptorelin':ti,ab,kw OR 'gnrh<br>antagonist':ti,ab,kw OR 'degarelix':ti,ab,kw<br>OR 'abiraterone':ti,ab,kw OR<br>'antiandrogen':ti,ab,kw OR<br>'bicalutamide':ti,ab,kw OR 'flutamide':ti,ab,kw<br>OR 'androgen deprivation':ti,ab,kw OR<br>'enzalutamide':ti,ab,kw OR<br>'apalutamide':ti,ab,kw OR<br>'darolutamide':ti,ab,kw OR<br>'docetaxel':ti,ab,kw OR 'cabazitaxel':ti,ab,kw<br>OR 'taxanes':ti,ab,kw OR<br>'ciproterone':ti,ab,kw OR 'olaparib':ti,ab,kw<br>OR 'radium':ti,ab,kw OR 'lutetium':ti,ab,kw OR<br>'diethylstilbestrol':ti,ab,kw OR 'ra-<br>223':ti,ab,kw OR 'lu-177':ti,ab,kw OR<br>'goserelin'/exp OR 'goserelin' OR<br>'leuprorelin'/exp OR 'leuprorelin' OR<br>'triptorelin'/exp OR 'triptorelin' OR<br>'gonadorelin'/exp OR 'gonadorelin' OR 'acetyl<br>2 naphthylalanyl 3 chlorophenylalanyl 1<br>oxohexadecyl seryl 4 aminophenylalanyl<br>hydroorotyl 4 aminophenylalanyl carbamoyl<br>leucyl ilys prolyl alaninamide'/exp OR 'acetyl 2<br>naphthylalanyl 3 chlorophenylalanyl 1<br>oxohexadecyl seryl 4 aminophenylalanyl<br>hydroorotyl 4 aminophenylalanyl carbamoyl<br>leucyl ilys prolyl alaninamide' OR 'abiraterone<br>acetate'/exp OR 'abiraterone acetate' OR<br>'abiraterone'/exp OR 'abiraterone' OR<br>'antiandrogen'/exp OR 'antiandrogen' OR<br>'bicalutamide'/exp OR 'bicalutamide' OR<br>'flutamide'/exp OR 'flutamide' OR<br>'enzalutamide'/exp OR 'enzalutamide' OR<br>'apalutamide'/exp OR 'apalutamide' OR<br>'darolutamide'/exp OR 'darolutamide' OR<br>'taxoid'/exp OR 'taxoid' OR 'docetaxel'/exp OR<br>'docetaxel' OR 'cabazitaxel'/exp OR<br>'cabazitaxel' OR 'olaparib'/exp OR 'olaparib'<br>OR 'radium'/exp OR 'radium' OR 'radium-233'<br>OR 'radium ra 223 dichloride'/exp OR 'radium<br>ra 223 dichloride' OR 'lutetium-177'/exp OR<br>'lutetium-177' OR 'diethylstilbestrol'/exp OR | 1337652    |

|                                     |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |
|-------------------------------------|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
|                                     |    | 'diethylstilbestrol' OR 'radiotherapy'/exp OR 'radiotherapy' OR 'zoladex':ti,ab,kw OR 'eligard':ti,ab,kw OR 'lupron':ti,ab,kw OR 'viadur':ti,ab,kw OR 'trelstar':ti,ab,kw OR 'firmagon':ti,ab,kw OR 'zytiga':ti,ab,kw OR 'orgovyx':ti,ab,kw OR 'plenaxis':ti,ab,kw OR 'casodex':ti,ab,kw OR 'eulexin':ti,ab,kw OR 'xtandi':ti,ab,kw OR 'erleada':ti,ab,kw OR 'nubeqa':ti,ab,kw OR 'androcur':ti,ab,kw OR 'jevtana':ti,ab,kw OR 'lynparza':ti,ab,kw OR 'distibene':ti,ab,kw OR 'honvol':ti,ab,kw OR 'stilbestrol':ti,ab,kw |         |
|                                     | 2  | 'prostatic' AND 'neoplasms' OR 'prostatic neoplasms' OR ('prostate' AND 'cancer') OR 'prostate cancer' OR 'prostate tumor'/exp OR 'prostatic neoplasms':ti,ab,kw OR 'neoplasm* prostatic':ti,ab,kw OR 'prostatic neoplasm*':ti,ab,kw OR 'neoplasm* prostate':ti,ab,kw OR 'prostate cancer':ti,ab,kw OR 'prostatic cancer*':ti,ab,kw OR 'cancer of prostate':ti,ab,kw                                                                                                                                                      | 402896  |
|                                     | 3  | #1 AND #2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 126622  |
|                                     | 4  | 'medline':ti,ab,kw OR ('systematic':ti,ab,kw AND 'review':ti,ab,kw) OR 'meta-analysis':it                                                                                                                                                                                                                                                                                                                                                                                                                                 | 614954  |
|                                     | 5  | 'randomized controlled trial':it OR 'randomized':ti,ab,kw OR 'placebo':ti,ab,kw                                                                                                                                                                                                                                                                                                                                                                                                                                           | 1500797 |
|                                     | 6  | #4 OR #5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1980848 |
|                                     | 7  | #3 AND #6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 13753   |
|                                     | 8  | #3 AND #4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 2970    |
|                                     | 9  | #3 AND ([controlled clinical trial]/lim OR [randomized controlled trial]/lim)                                                                                                                                                                                                                                                                                                                                                                                                                                             | 8310    |
|                                     | 10 | #8 OR #9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 11138   |
|                                     | 11 | 'randomized controlled trial':it OR ('randomized':ti,ab,kw AND 'controlled':ti,ab,kw AND 'trial':ti,ab,kw)                                                                                                                                                                                                                                                                                                                                                                                                                | 379181  |
|                                     | 12 | #4 OR #11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 971047  |
|                                     | 13 | #3 AND #11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 1618    |
|                                     | 14 | #3 AND #12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 4446    |
| Número de referencias identificadas |    | <b>4446</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |         |

Fuente: elaboración propia.

**Tabla D-3. Estrategia de búsqueda Cochrane**

| Característica                      | Reporte     |                                                                                                                                                                                           |            |
|-------------------------------------|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Tipo de búsqueda                    | Nueva       |                                                                                                                                                                                           |            |
| Bases de datos                      | Cochrane    |                                                                                                                                                                                           |            |
| Plataforma                          | CENTRAL     |                                                                                                                                                                                           |            |
| Fecha de búsqueda                   | 26/06/2025  |                                                                                                                                                                                           |            |
| Rango de fecha de búsqueda          | Ninguna     |                                                                                                                                                                                           |            |
| Restricciones de lenguaje           | Ninguna     |                                                                                                                                                                                           |            |
| Otros límites                       | Ninguna     |                                                                                                                                                                                           |            |
| Estrategia de búsqueda              | #           | Búsqueda                                                                                                                                                                                  | Resultados |
|                                     | 1           | (luteinizing Hormone Releasing Hormone Agonist):ti,ab,kw OR (Gonadotropin Releasing Hormone Agonist):ti,ab,kw OR (LHRH agonist):ti,ab,kw OR (Goserelin):ti,ab,kw OR (Leuprolide):ti,ab,kw | 3718       |
|                                     | 2           | (leuproreline):ti,ab,kw OR (Triptorelin):ti,ab,kw OR (GnRH antagonist):ti,ab,kw OR (Degarelix):ti,ab,kw OR (abiraterone):ti,ab,kw                                                         | 4110       |
|                                     | 3           | (antiandrogen):ti,ab,kw OR (bicalutamide):ti,ab,kw OR (flutamide):ti,ab,kw OR (androgen deprivation):ti,ab,kw AND (Enzalutamide):ti,ab,kw                                                 | 1899       |
|                                     | 4           | (apalutamide):ti,ab,kw OR (Darolutamide):ti,ab,kw OR (taxanes):ti,ab,kw OR (taxoids):ti,ab,kw OR (Docetaxel):ti,ab,kw                                                                     | 10431      |
|                                     | 5           | (Ciproterone):ti,ab,kw OR (Cabazitaxel):ti,ab,kw OR (Olaparib):ti,ab,kw OR (Radium):ti,ab,kw OR (Lutetium):ti,ab,kw                                                                       | 2018       |
|                                     | 6           | (Diethylstilbestrol):ti,ab,kw                                                                                                                                                             | 316        |
|                                     | 7           | #1 OR #2 OR #3 OR #4 OR #5 OR #6                                                                                                                                                          | 19236      |
|                                     | 8           | (prostatic):ti,ab,kw AND (neoplasm*):ti,ab,kw                                                                                                                                             | 9374       |
|                                     | 9           | (prosta*):ti,ab,kw AND (cancer):ti,ab,kw                                                                                                                                                  | 18956      |
|                                     | 10          | (prosta*):ti,ab,kw AND (carcino*):ti,ab,kw                                                                                                                                                | 1941       |
|                                     | 11          | #8 OR #9 OR #10                                                                                                                                                                           | 20105      |
|                                     | 12          | #7 AND #11 – Clinical Trials                                                                                                                                                              | 5203       |
|                                     | 13          | #7 AND #11 – Cochrane Reviews                                                                                                                                                             | 6          |
| Número de referencias identificadas | <b>5209</b> |                                                                                                                                                                                           |            |

Fuente: elaboración propia.

**Tabla D-4. Estrategia de búsqueda en LILACS**

| Característica                      | Reporte                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
|-------------------------------------|------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Tipo de búsqueda                    | Nueva                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Bases de datos                      | LILACS                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Plataforma                          | BVSsalud                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Fecha de búsqueda                   | 26/06/2026                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Rango de fecha de búsqueda          | Ninguna                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Restricciones de lenguaje           | Ninguna                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Otros límites                       | Revisiones sistemáticas y metaanálisis<br>Ensayos clínicos |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Estrategia de búsqueda              | Nº                                                         | Búsqueda                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Resultados |
|                                     | 1                                                          | ((Goserelina) OR (Leuprolida) OR (Triptorelin) OR (Degarelix) OR (abiraterona) OR (bicalutamida) OR (flutamida) OR (Enzalutamida) OR (apalutamida) OR (Darolutamida) OR (Docetaxel) OR (Ciproterona) OR (Cabazitaxel) OR (Olaparib) OR (radio) OR (Lutecio) OR (dietilbestrol)) AND (((prostata) AND (cancer)) OR ((prosta*) AND (neop*)))                                                                                                                                                                                                                                                           | 20033      |
|                                     | 2                                                          | (((prostata) AND (cancer)) OR ((prosta*) AND (neop*)))                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 15332      |
|                                     | 3                                                          | ((Goserelina) OR (Leuprolida) OR (Triptorelin) OR (Degarelix) OR (abiraterona) OR (bicalutamida) OR (flutamida) OR (Enzalutamida) OR (apalutamida) OR (Darolutamida) OR (Docetaxel) OR (Ciproterona) OR (Cabazitaxel) OR (Olaparib) OR (radio) OR (Lutecio) OR (dietilbestrol)) AND (((prostata) AND (cancer)) OR ((prosta*) AND (neop*)))                                                                                                                                                                                                                                                           | 539        |
|                                     | 4                                                          | ((goserelina) OR (leuprolida) OR (triptorelin) OR (degarelix) OR (abiraterona) OR (bicalutamida) OR (flutamida) OR (enzalutamida) OR (apalutamida) OR (darolutamida) OR (docetaxel) OR (ciproterona) OR (cabazitaxel) OR (olaparib) OR (radio) OR (lutecio) OR (dietilbestrol)) AND (((prostata) AND (cancer)) OR ((prosta*) AND (neop*))) AND type_of_study:("literature_review" OR "guideline" OR "clinical_trials" OR "evaluation_studies" OR "health_technology_assessment" OR "health_economic_evaluation" OR "systematic_reviews" OR "sysrev_observational_studies") AND instance:"lilacsplus" | 199        |
| Número de referencias identificadas |                                                            | 199                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |

Fuente: elaboración propia

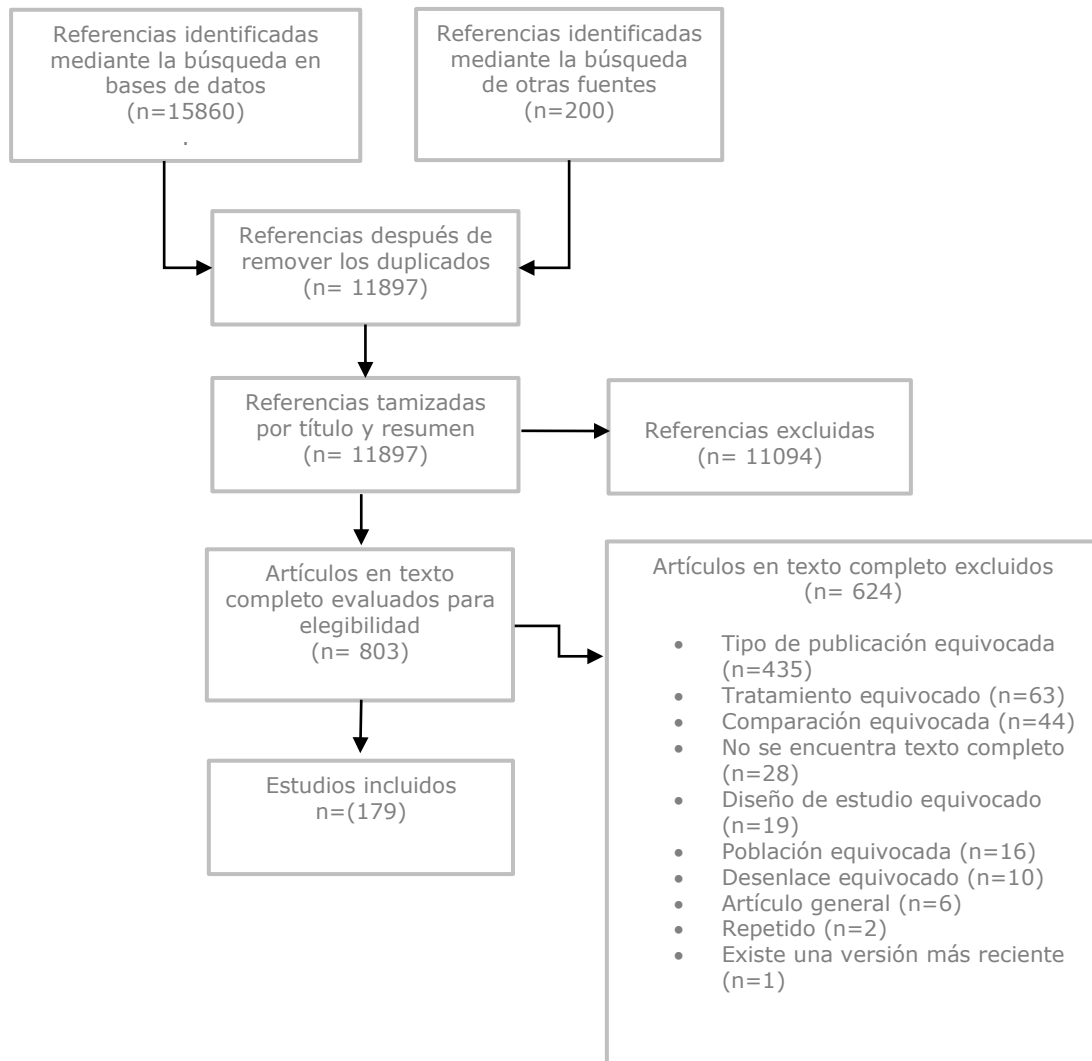
**Tabla D-5. Estrategia de búsqueda en Google Scholar**

| Característica                      | Reporte                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Tipo de búsqueda                    | Nueva                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |            |
| Bases de datos                      | Google Scholar                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |            |
| Plataforma                          | Google Scholar                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |            |
| Fecha de búsqueda                   | 26/06/2025                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Rango de fecha de búsqueda          | Ninguna                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Restricciones de lenguaje           | Ninguna                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| Otros límites                       | Revisiones sistemáticas y metaanálisis<br>Ensayos clínicos                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |
| Estrategia de búsqueda              | Búsqueda                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Resultados |
|                                     | LHRH agonist OR Goserelin OR Leuprolide OR Triptorelin OR GnRH antagonist OR Degarelix OR abiraterone OR relugolix OR abarelix OR antiandrogen OR bicalutamide OR flutamide OR nilutamide OR androgen deprivation OR Enzalutamide OR apalutamide OR Darolutamide OR Estrogen OR taxanes OR Docetaxel OR Ciproterone OR Cabazitaxel OR Mitoxantrone OR Olaparib OR Rucaparib OR Talazoparib OR Niraparib OR Radium OR Lutetium OR Diethylstilbestrol OR Taxoids                                                                               | 32800      |
|                                     | prostatic neoplasm OR prostate cancer OR prostatic cancer OR prostate                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 821000     |
|                                     | (prostatic neoplasm OR prostate cancer OR prostatic cancer OR prostate) AND (LHRH agonist OR Goserelin OR Leuprolide OR Triptorelin OR GnRH antagonist OR Degarelix OR abiraterone OR relugolix OR abarelix OR antiandrogen OR bicalutamide OR flutamide OR nilutamide OR androgen deprivation OR Enzalutamide OR apalutamide OR Darolutamide OR Estrogen OR taxanes OR Docetaxel OR Ciproterone OR Cabazitaxel OR Mitoxantrone OR Olaparib OR Rucaparib OR Talazoparib OR Niraparib OR Radium OR Lutetium OR Diethylstilbestrol OR Taxoids) | 12500      |
| Número de referencias identificadas | <b>200</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |            |

Fuente: elaboración propia.

## **Anexo E. Diagrama de flujo PRISMA para la búsqueda de efectividad y seguridad**

**Figura E-1. Diagrama Prisma (para ensayos clínicos y revisiones sistemáticas)**



## Anexo F. Listado de estudios incluidos en esta revisión

**Tabla F-1. Listado de estudios incluidos en la revisión**

| Autor                                                                                                                                                                                                                         | Título                                                                                                                                                                          | Revista                             | Año  | Volumen | Número | Página  | Tipo de estudio                               | Pregunta |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|------|---------|--------|---------|-----------------------------------------------|----------|
| Schellhammer, P and Sharifi, R and Block, N and Soloway, M and Venner, P and Patterson, A L and Sarosdy, M and Vogelzang, N and Jones, J and Kolvenbag, G                                                                     | A controlled trial of bicalutamide versus flutamide, each in combination with luteinizing hormone-releasing hormone analogue therapy, in patients with advanced prostate cancer | Urology                             | 1995 | 45      | 5      | 745-752 | Ensayo clínico                                | P3       |
| K, Fizazi and N, Tran and L, Fein and N, Matsubara and A, Rodriguez-Antolin and BY, Alekseev and M, Özgüroğlu and D, Ye and S, Feyerabend and A, Protheroe and P, De Porre and T, Kheoh and YC, Park and MB, Todd and KN, Chi | Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer.                                                                                                | The New England journal of medicine | 2017 | 377     | 4      | 352-360 | Ensayo clínico                                | P3       |
| SS, Wang and XJ, Bian and JL, Wu and BH, Wang and S, Zhang and DW, Ye                                                                                                                                                         | Network meta-analysis of combination strategies in metastatic hormone-sensitive prostate cancer.                                                                                | Asian journal of andrology          | 2024 | 26      | 4      | 402-408 | Revisión sistemática con meta análisis en red | P3       |
| K, Mori and H, Mostafaei and R, Sari Motlagh and B, Pradere and F, Qahal and E, Laukhtina and VM, Schuettfort and G, Kramer                                                                                                   | Systemic therapies for metastatic hormone-sensitive prostate cancer: network meta-analysis.                                                                                     | BJU international                   | 2022 | 129     | 4      | 423-433 | Revisión sistemática con meta análisis en red | P3       |



| Autor                                                                                                                                                                                                                                                                                                                     | Título                                                                                                                                                                                                                                                                                  | Revista                                             | Año  | Volumen | Número | Página        | Tipo de estudio                                     | Pregunta |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|------|---------|--------|---------------|-----------------------------------------------------|----------|
| and M, Abufaraj and PI, Karakiewicz and T, Kimura and S, Egawa and SF, Shariat                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                         |                                                     |      |         |        |               |                                                     |          |
| H, Mutlu and H, Bozcuk                                                                                                                                                                                                                                                                                                    | The optimal upfront therapy in metastatic hormone-sensitive prostate cancer: A network meta-analysis.                                                                                                                                                                                   | Journal of cancer research and therapeutics         | 2023 | 19      | 2      | 394-402       | Revisión sistemática con meta análisis en red       | P3       |
| M, Ferro and G, Lucarelli and F, Crocetto and P, Dolce and A, Verde and E, La Civita and S, Zappavigna and de Cobelli O and G, Di Lorenzo and BA, Facchini and L, Scafuri and L, Onofrio and A, Porreca and GM, Busetto and G, Sonpavde and M, Caraglia and M, Klain and D, Terracciano and S, De Placido and C, Buonerba | First-line systemic therapy for metastatic castration-sensitive prostate cancer: An updated systematic review with novel findings.                                                                                                                                                      | Critical reviews in oncology/hematology             | 2021 | 157     |        | 103198-103198 | Revisión sistemática con meta análisis convencional | P3       |
| MA, Climent and A, Font and I, Durán and J, Puente and M, José Méndez-Vidal and MI, Sáez and C, Santander Lobera and J, Ángel Arranz Arika and A, González-Del-                                                                                                                                                           | A phase II randomised trial of abiraterone acetate plus prednisone in combination with docetaxel or docetaxel plus prednisone after disease progression to abiraterone acetate plus prednisone in patients with metastatic castration-resistant prostate cancer: The ABIDO-SOGUG trial. | European journal of cancer (Oxford, England : 1990) | 2022 | 175     |        | 110-119       | Ensayo clínico                                      | P4       |

| Autor                                                                                                                                                                                                                                | Título                                                                                                                                                                                                                                                        | Revista | Año | Volumen | Número | Página | Tipo de estudio | Pregunta |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|-----|---------|--------|--------|-----------------|----------|
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| and A, Rodriguez Antolin                                                                                                                                                                                                                |                                                                                                                                                                                       |                                                     |      |         |        |         |                                               |          |
| Huang, Y and He, H and Liang, L and Zhang, Y and Peng, K and Wang, Y and Wu, J and Long, X and Kairemo, K and Goldberg, H and LC, Mendez and Gu, D                                                                                      | Efficacy and safety of PARP inhibitors in the treatment of prostatic cancer: a systematic review and network meta-analysis. PG - 64 LID - 10.21037/cco-24-82 [doi]                    |                                                     |      |         | 2304   |         | Revisión sistemática con meta análisis en red | P4       |
| GT, Bales and GW, Chodak                                                                                                                                                                                                                | A controlled trial of bicalutamide versus castration in patients with advanced prostate cancer. PG - 38-43; discussion 48-53                                                          |                                                     |      |         | 90     |         | Ensayo clínico                                | P4       |
| Gomez-Veiga, F and Szmulewitz, R Z and Holzbeierlein, J and Azad, A A and Iguchi, T and Villers, A and Alcaraz, A and Alekseev, B and Shore, N D and Rosbrook, B and Zohren, F and Ma, J and Haas, G P and Stenzl, A and Armstrong, A J | Clinical Outcomes of Enzalutamide in Metastatic Hormone-sensitive Prostate Cancer in Patients Aged <75 and ≥75 Years: ARCHES Post Hoc Analysis                                        | European Urology Oncology                           | 2024 | 7       | 4      | 860-869 | Ensayo clínico                                | P3       |
| O, Caffo and C, Ortega and F, Nolè and D, Gasparro and C, Mucciarini and M, Aieta and V, Zagonel and R, Iacovelli and U, De Giorgi and G, Facchini and A,                                                                               | Docetaxel and prednisone with or without enzalutamide as first-line treatment in patients with metastatic castration-resistant prostate cancer: CHEIRON, a randomised phase II trial. | European journal of cancer (Oxford, England : 1990) | 2021 | 155     |        | 56-63   | Ensayo clínico                                | P4       |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Título                                                                                                                                                                                 | Revista                                       | Año  | Volumen | Número | Página  | Tipo de estudio   | Pregunta |
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| H, Uemura and<br>H, Matsushima<br>and K, Kobayashi<br>and H, Mizusawa<br>and H,<br>Nishimatsu and<br>K, Fizazi and M,<br>Smith and N,<br>Shore and T,<br>Tammela and KI,<br>Tabata and N,<br>Matsubara and M,                                                                                                                                                                                                                                                                                                                                                                 | Efficacy and safety of<br>darolutamide in Japanese patients<br>with nonmetastatic castration-<br>resistant prostate cancer: a sub-<br>group analysis of the phase III<br>ARAMIS trial. | International journal<br>of clinical oncology | 2021 | 26      | 3      | 578-590 | Ensayo<br>clínico | P2       |



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| AE, Hird and DE, Magee and B, Bhindi and XY, Ye and T, Chandrasekar and H, Goldberg and L, Klotz and N, Fleshner and R, Satkunasivam and Z, Klaassen and CJD, Wallis                 | A Systematic Review and Network Meta-analysis of Novel Androgen Receptor Inhibitors in Non-metastatic Castration-resistant Prostate Cancer.                                                 | Clinical genitourinary cancer          | 2020 | 18      | 5      | 343-350   | Revisión sistemática con meta análisis en red | P2       |
| S, Fukasawa and H, Suzuki and K, Kawaguchi and H, Noguchi and K, Enjo and N, Tran and M, Todd                                                                                        | Efficacy and safety of abiraterone acetate plus prednisone in Japanese patients with newly diagnosed, metastatic hormone-naïve prostate cancer: a subgroup analysis of LATITUDE, a          | Japanese journal of clinical oncology  | 2018 | 48      | 11     | 1012-1021 | Ensayo clínico                                | P3       |

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| and K, Fizazi and N, Matsubara                                                                                                                                                                                                                                                                                           | randomized, double-blind, placebo-controlled, Phase 3 study.                                                                    |                                  |      |         |        |             |                                               |          |
| YS, Pu and H, Ahn and W, Han and SP, Huang and HC, Wu and L, Ma and S, Yamada and K, Suga and LP, Xie                                                                                                                                                                                                                    | Enzalutamide in Chemotherapy-Naïve Metastatic Castration-Resistant Prostate Cancer: An Asian Multiregional, Randomized Study.   | Advances in therapy              | 2022 | 39      | 6      | 2641-2656   | Ensayo clínico                                | P4       |
| Iregui Parra, J D and García-Perdomo, H A                                                                                                                                                                                                                                                                                | Treatment of non-metastatic castration-resistant prostate cancer: A systematic review and network meta-analysis                 | Revista Mexicana de Urologia     | 2024 | 84      | 3      |             | Revisión sistemática con meta análisis en red | P2       |
| Yokomizo, A and Shiota, M and Morokuma, F and Eto, M and Matsuyama, H and Matsumoto, H and Kamoto, T and Terada, N and Kawahara, K and Enokida, H and Tatarano, S and Fujimoto, N and Higashijima, K and Sakai, H and Hakariya, T and Igawa, T and Suekane, S and Kamba, T and Sugiyama, Y and Kishimoto, J and Naito, S | GnRH antagonist monotherapy versus a GnRH agonist plus bicalutamide for advanced hormone-sensitive prostate cancer; KYUCOG-1401 | International Journal of Urology | 2024 | 31      | 4      | 362-369     | Ensayo clínico                                | P3       |
| Dittono, F and Bianchi, A and Malandra, S and Porcaro, A B and Fantinel, E and Negrelli, R and Ferro, M and                                                                                                                                                                                                              | PARP Inhibitors in Metastatic Prostate Cancer: A Comprehensive Systematic Review and Meta-analysis of Existing Evidence         | Clinical Genitourinary Cancer    | 2024 | 22      | 2      | 402-412.e17 | Revisión sistemática con meta análisis en red | P4       |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                            | Título                                                                                                                                                                                                                                                       | Revista                                                                                      | Año  | Volumen | Número | Página    | Tipo de estudio                               | Pregunta |
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| Xiong, X and Zhang, S and Zheng, W and Liao, X and Yang, J and Xu, H and Hu, S and Wei, Q and Yang, L                                                                                                                                                                                                                                                                                                                            | Second-line treatment options in metastatic castration-resistant prostate cancer after progression on first-line androgen-receptor targeting therapies: A systematic review and Bayesian network analysis. PG - 104286 LID - S1040-8428(24)00029-5 [pii] LID |                                                                                              |      |         | 1879   |           | Revisión sistemática con meta análisis en red | P4       |
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| Wang and TM,<br>Beer and ES,<br>Antonarakis                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                               |                                                     |      |         |        |               |                                               |          |
| KN, Chi and<br>Protheroe, A and<br>Rodríguez-<br>Antolín, A and<br>Facchini, G and<br>Suttman, H and<br>Matsubara, N and<br>Ye, Z and Keam,<br>B and Damião, R<br>and Li, T and<br>McQuarrie, K and<br>Jia, B and P, De<br>Porre and Martin,<br>J and MB, Todd<br>and Fizazi, K | Patient-reported outcomes following abiraterone acetate plus prednisone added to androgen deprivation therapy in patients with newly diagnosed metastatic castration-naïve prostate cancer (LATITUDE): an international, randomised phase 3 trial. PG - 194-2 |                                                     |      |         | 1474   |               | Ensayo clínico                                | P3       |
| A, Nabid and N,<br>Carrier and E,<br>Vigneault and T,<br>Van Nguyen and<br>P, Vavassis and<br>MA, Brassard and<br>B, Bahoric and R,<br>Archambault and<br>F, Vincent and R,<br>Bettahar and D,<br>Wilke and L,<br>Souhami                                                       | Androgen deprivation therapy and radiotherapy in intermediate-risk prostate cancer: A randomised phase III trial.                                                                                                                                             | European journal of cancer (Oxford, England : 1990) | 2021 | 143     |        | 64-74         | Ensayo clínico                                | P1       |
| J, Cassinello and<br>T, Domínguez-<br>Lubillo and M,<br>Gómez-Barrera<br>and T, Hernando<br>and R, Parra and<br>I, Asensio and<br>MA, Casado and<br>P, Moreno                                                                                                                   | Optimal treatment sequencing of abiraterone acetate plus prednisone and enzalutamide in patients with castration-resistant metastatic prostate cancer: A systematic review and meta-analysis.                                                                 | Cancer treatment reviews                            | 2021 | 93      |        | 102152-102152 | Revisión sistemática con meta análisis en red | P4       |
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| Crawford, E D and Eisenberger, M A and McLeod, D G and                                                                                                                                                                                                                                                                                                                                                                                      | A controlled trial of leuprolide with and without flutamide in prostatic carcinoma                                                                                                 | New England Journal of Medicine      | 1989 | 321     | 7      | 419-424   | Ensayo clínico       | P3       |

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| Suzuki, H and Castellano, D and De Bono, J and Sternberg, C N and Fizazi, K and Tombal, B and Wulfing, C and Foster, M C and Ozatilgan, A and Geffriaud-Ricouard, C and al., et | Cabazitaxel versus abiraterone or enzalutamide in metastatic castration-resistant prostate cancer: post hoc analysis of the CARD study excluding chemohormonal therapy for castrate-naive disease | Japanese journal of clinical oncology                                              | 2021 | 51      | 8      | 1287-1297 | Ensayo clínico                                | P4       |
| Zhang, D and Weng, H and Zhu, Z and Gong, W and Ma, Y                                                                                                                           | Evaluating first-line therapeutic strategies for metastatic castration-resistant prostate cancer: a comprehensive network meta-analysis and systematic review                                     | Frontiers in Oncology                                                              | 2024 | 14      |        |           | Revisión sistemática con meta análisis en red | P4       |
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| S, Chowdhury and S, Oudard and H, Uemura and S, Joniau and D, Pilon and P, Lefebvre and K, McQuarrie and J, Liu and L,                                                          | Matching-Adjusted Indirect Comparison of Health-Related Quality of Life and Adverse Events of Apalutamide Versus Enzalutamide in Non-Metastatic Castration-Resistant Prostate Cancer.             | Advances in therapy                                                                | 2020 | 37      | 1      | 512-526   | Revisión sistemática con meta análisis en red | P2       |

| Autor                                                                                                                                                                            | Título                                                                                                                                                                                                                                                      | Revista                                                                            | Año  | Volumen | Número | Página  | Tipo de estudio                                     | Pregunta |
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| Yan, K and Balijepalli, C and Gullapalli, L and Joshy, J and Kotum, S and Druyts, E                                                                                              | Efficacy and safety of interventions for metastatic castration resistant prostate cancer (mCRPC) patients progressing on androgen receptor-axis-targeted (ARAT) therapy: a systematic literature review. PG - 1741-1752 LID - 10.1080/03007995.2024.2395435 |                                                                                    |      |         | 1473   |         | Revisión sistemática con meta análisis convencional | P4       |
| Heidenreich, A and Chowdhury, S and Klotz, L and Siemens, D R and Villers, A and Ivanescu, C and Holmstrom, S and Baron, B and Wang, F and Lin, P and al., et                    | Impact of Enzalutamide Compared with Bicalutamide on Quality of Life in Men with Metastatic Castration-resistant Prostate Cancer: additional Analyses from the TERRAIN Randomised Clinical Trial                                                            | European urology                                                                   | 2017 | 71      | 4      | 534-542 | Ensayo clínico                                      | P4       |
| J, Kumar and SB, Jazayeri and S, Gautam and D, Norez and MU, Alam and K, Tanneru and S, Bazargani and J, Costa and M, Bandyk and HP, Ganapathi and S, Koochehpour and KC, Balaji | Comparative efficacy of apalutamide darolutamide and enzalutamide for treatment of non-metastatic castrate-resistant prostate cancer: A systematic review and network meta-analysis.                                                                        | Urologic oncology                                                                  | 2020 | 38      | 11     | 826-834 | Revisión sistemática con meta análisis en red       | P2       |
| D, Cella and C, Ivanescu and S, Holmstrom and CN, Bui and J,                                                                                                                     | Impact of enzalutamide on quality of life in men with metastatic castration-resistant prostate cancer after chemotherapy:                                                                                                                                   | Annals of oncology : official journal of the European Society for Medical Oncology | 2015 | 26      | 1      | 179-185 | Ensayo clínico                                      | P4       |



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| AA, Azad and DP, Petrylak and T, Iguchi and ND, Shore and A, Villers and F, Gomez-Veiga and A, Alcaraz and B, Alekseev and RZ, Szmulewitz and J, Holzbeierlein and B, Rosbrook and J, Ma and F, Zohren and NN, El-Chaar and GP, Haas and A, Stenzl and AJ, Armstrong                                                          | Enzalutamide and Prostate-Specific Antigen Levels in Metastatic Prostate Cancer: A Secondary Analysis of the ARCHES Randomized Clinical Trial.                | JAMA network open                                                                            | 2025 | 8       | 5      | e258751-e258751 | Ensayo clínico  | P3       |

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| TH, Lee and H, Pyo and GS, Yoo and JH, Kim and SS, Jeon and SI, Seo and BC, Jeong and HG, Jeon and HH, Sung and M, Kang and W, Song and JH, Chung and W, Park                   | Androgen deprivation alone versus combined with pelvic radiation for adverse events and quality of life in clinically node-positive prostate cancer.                                                                                   | Scientific reports                   | 2024 | 14      | 1      | 8207-8207 | Ensayo clínico                                | P1       |
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| S, Oudard and B, Hadaschik and F, Saad and D, Cella and E, Basch and                                                                                                            | Health-related Quality of Life at the SPARTAN Final Analysis of Apalutamide for Nonmetastatic Castration-resistant Prostate                                                                                                            | European urology focus               | 2022 | 8       | 4      | 958-967   | Ensayo clínico                                | P2       |

| Autor                                                                                                                                                                                                                                                                                                                                                                         | Título                                                                                                                                                                       | Revista                     | Año  | Volumen | Número | Página    | Tipo de estudio | Pregunta |
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| Satapathy, S and Mittal, B R and Sood, A and Das, C K and Mavuduru, R S and Goyal, S and Shukla, J and Singh, S K                                                                                                                                                                                                                                                             | [177Lu]Lu-PSMA-617 Versus Docetaxel in Chemotherapy-Naïve Metastatic Castration-Resistant Prostate Cancer: final Survival Analysis of a Phase 2 Randomized, Controlled Trial | Journal of nuclear medicine | 2023 | 64      | 11     | 1726-1729 | Ensayo clínico  | P4       |
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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|------|---------|--------|-------------|----------------------|----------|
| Santana Gomes, A J and Given, R and Juárez Soto, Á and Merseburger, A S and Özgüroğlu, M and Uemura, H and al., et                                                                   |                                                                                                                                                                |                                 |      |         |        |             |                      |          |
| Smith, M R and Saad, F and Chowdhury, S and Oudard, S and Hadaschik, B A and Graff, J N and Olmos, D and Mainwaring, P N and Lee, J Y and Uemura, H and al., et                      | Apalutamide Treatment and Metastasis-free Survival in Prostate Cancer                                                                                          | New England journal of medicine | 2018 | 378     | 15     | 1408-1418   | Ensayo clínico       | P2       |
| Kumar, J and Gautam, S and Norez, D and Alam, M U and Tanneru, K and Jazayeri, S B and Bazargani, S and Ganapathi, H P and Bandyk, M and Costa, J and Koochekpour, S and Balaji, K C | Comparative efficacy of enzalutamide, apalutamide and darolutamide for treatment on non-metastatic castrate-resistant prostate cancer: a network meta-analysis | Journal of Urology              | 2020 | 203     |        | e1217-e1217 | Revisión sistemática | P2       |
| Sathianathan, N J and Koschel, S and Thangasamy, I A and Teh, J and Alghazo, O and Butcher, G and Howard, H and Kapoor, J and Lawrentschuk, N and Siva, S and                        | Indirect Comparisons of Efficacy between Combination Approaches in Metastatic Hormone-sensitive Prostate Cancer: A Systematic Review and Network Meta-analysis | European Urology                | 2020 | 77      | 3      | 365-372     | Revisión sistemática | P3       |

| Autor                                                                                                                                                                  | Título                                                                                                                                                                                   | Revista                         | Año  | Volumen | Número | Página    | Tipo de estudio      | Pregunta |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|------|---------|--------|-----------|----------------------|----------|
| Azad, A and Tran, B and Bolton, D and Murphy, D G                                                                                                                      |                                                                                                                                                                                          |                                 |      |         |        |           |                      |          |
| Di Nunno, V and Santoni, M and Mollica, V and Conti, A and Montironi, R and Battelli, N and Ardizzoni, A and Massari, F                                                | Systemic Treatment for Metastatic Hormone Sensitive Prostate Cancer: A Comprehensive Meta-Analysis Evaluating Efficacy and Safety in Specific Sub-Groups of Patients                     | Clinical Drug Investigation     | 2020 | 40      | 3      | 211-226   | Revisión sistemática | P3       |
| Davis, I D and Martin, A J and Stockler, M R and Begbie, S and Chi, K N and Chowdhury, S and Coskinas, X and Frydenberg, M and Hague, W E and Horvath, L G and al., et | Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer                                                                                                              | New England journal of medicine | 2019 | 381     | 2      | 121-131   | Ensayo clínico       | P3       |
| Armstrong, A J and Lin, P and Tombal, B and Saad, F and Higano, C S and Joshua, A M and Parli, T and Rosbrook, B and van Os, S and Beer, T M                           | Five-year Survival Prediction and Safety Outcomes with Enzalutamide in Men with Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer from the PREVAIL Trial                | European urology                | 2020 | 78      | 3      | 347-357   | Ensayo clínico       | P4       |
| Mason, M D and Parulekar, W R and Sydes, M R and Brundage, M and Kirkbride, P and Gospodarowicz, M and Cowan, R and Kostashuk, E C and Anderson,                       | Final report of the intergroup randomized study of combined androgen-deprivation therapy plus radiotherapy versus androgen-deprivation therapy alone in locally advanced prostate cancer | Journal of Clinical Oncology    | 2015 | 33      | 19     | 2143-2150 | Ensayo clínico       | P1       |

| Autor                                                                                                                                                                                                                          | Título                                                                                                                                                                                        | Revista            | Año  | Volumen | Número | Página  | Tipo de estudio | Pregunta |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|------|---------|--------|---------|-----------------|----------|
| J and Swanson, G and Parmar, M K B and Hayter, C and Jovic, G and Hiltz, A and Hetherington, J and Sathya, J and Barber, J B P and McKenzie, M and El-Sharkawi, S and Souhami, L and Hardman, P D J and Chen, B E and Warde, P |                                                                                                                                                                                               |                    |      |         |        |         |                 |          |
| Khalaf, D J and Sunderland, K and Eigl, B J and Kollmannsberger, C K and Ivanov, N and Finch, D L and Oja, C and Vergidis, J and Zulfiqar, M and Gleave, M E and al., et                                                       | Health-related Quality of Life for Abiraterone Plus Prednisone Versus Enzalutamide in Patients with Metastatic Castration-resistant Prostate Cancer: results from a Phase II Randomized Trial | European urology   | 2019 | 75      | 6      | 940-947 | Ensayo clínico  | P4       |
| Evans, C P and Higano, C S and Keane, T and Andriole, G and Saad, F and Iversen, P and Miller, K and Kim, C S and Kimura, G and Armstrong, A J and al., et                                                                     | The PREVAIL Study: primary Outcomes by Site and Extent of Baseline Disease for Enzalutamide-treated Men with Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer               | European urology   | 2016 | 70      | 4      | 675-683 | Ensayo clínico  | P4       |
| Siemens, D R and Klotz, L and Heidenreich, A and Chowdhury, S and Villers, A and Baron, B and van Os, S and                                                                                                                    | Efficacy and Safety of Enzalutamide vs Bicalutamide in Younger and Older Patients with Metastatic Castration Resistant Prostate Cancer in the TERRAIN Trial                                   | Journal of urology | 2018 | 199     | 1      | 147-154 | Ensayo clínico  | P4       |

| Autor                                                                                                                                                                | Título                                                                                                                                                 | Revista                             | Año  | Volumen | Número | Página          | Tipo de estudio                               | Pregunta |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|------|---------|--------|-----------------|-----------------------------------------------|----------|
| Hasabou, N and Wang, F and Lin, P and al., et                                                                                                                        |                                                                                                                                                        |                                     |      |         |        |                 |                                               |          |
| Von Buren, M and Armstrong, A J and Szmulewitz, R and Petrylak, D and Villers, A and Azad, A and Alcaraz, A and Alekseev, B and Iguchi, T and Shore, N D and al., et | Androgen deprivation therapy with enzalutamide or placebo in metastatic hormone-sensitive prostate cancer: ARCHES                                      | Swiss medical weekly                | 2019 | 149     |        | 16S-16S         | Ensayo clínico                                | P3       |
| Hoeh, B and Wenzel, M and Tian, Z and Karakiewicz, P I and Saad, F and Steuber, T and Graefen, M and Tilki, D and Herout, R and Thomas, C and al., et                | Triplet or Doublet Therapy in Metastatic Hormone-sensitive Prostate Cancer Patients: an Updated Network Meta-analysis Including ARANOTE Data           | European urology focus              | 2024 |         |        |                 | Revisión sistemática                          | P3       |
| De Bono, J S and Sartor, O and Geffriaud-Ricouard, C and Joulain, F and Widmark, A                                                                                   | Cabazitaxel shows a consistently greater survival benefit compared to mitoxantrone in patients with mCRPC                                              | Nowotwory                           | 2014 | 64      | 1      | 1-6             | Ensayo clínico                                | P4       |
| Liu, Y and Deng, X and Wen, Z and Huang, J and Wang, C and Chen, C and Bao, E and Wang, J and Yang, X                                                                | Comparing efficacy of first-line treatment of metastatic castration resistant prostate cancer: a network meta-analysis of randomized controlled trials | Frontiers in pharmacology           | 2023 | 14      |        | 1290990-1290990 | Revisión sistemática con meta análisis en red | P4       |
| M, Hussain and J, Mateo and K, Fizazi and F, Saad and N,                                                                                                             | Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer.                                                                             | The New England journal of medicine | 2020 | 383     | 24     | 2345-2357       | Revisión sistemática con meta                 | P4       |



| Autor                                                                                                                                                                                                                                       | Título | Revista | Año | Volumen | Número | Página | Tipo de estudio       | Pregunta |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|---------|-----|---------|--------|--------|-----------------------|----------|
| Shore and S, Sandhu and KN, Chi and O, Sartor and N, Agarwal and D, Olmos and A, Thiery-Vuillemin and P, Twardowski and G, Roubaud and M, Özgüroğlu and J, Kang and J, Burgents and C, Gresty and C, Corcoran and CA, Adelman and de Bono J |        |         |     |         |        |        | análisis convencional |          |

## Anexo G. Listado de estudios excluidos en esta revisión

**Tabla G-1. Listado de estudios excluidos en la revisión**

| Autor                                                                                                                                                                                       | Título                                                                                                                                                                                                               | Revista                         | Año  | Volumen | Número | Páginas       | Razón de exclusión             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|------|---------|--------|---------------|--------------------------------|
| Suttman, H and Mulders, P F A and Molina, A and Goodman Jr, O B and Flaig, T W and Li, J and Kheoh, T and De Bono, J S and Scher, H I                                                       | Exploratory analysis of the visceral disease patient subset in COU-AA-301, a phase III study of abiraterone acetate (AA) in metastatic castration-resistant prostate cancer (mCRPC)                                  | European urology, supplements   | 2013 | 12      | 1      | e105-e106     | Tipo de publicación equivocada |
| Roach III, M                                                                                                                                                                                | Radiotherapy plus adjuvant goserelin improves survival in men with poor prognosis prostate cancer                                                                                                                    | Cancer treatment reviews        | 2005 | 31      | 7      | 582-586       | Tipo de publicación equivocada |
| Chi, K N and Chowdhury, S and Bjartell, A and Chung, B H and Given, R and Pereira de Santana Gomes, A J and Jurarez Soto, A and Merseburger, A S and Ozguroglu, O and Uemura, H and al., et | Final analysis results from TITAN: a phase 3 study of apalutamide (APA) vs placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) receiving androgen deprivation therapy (ADT) | Oncology research and treatment | 2021 | 44      |        | 74-74         | Tipo de publicación equivocada |
| Efstathiou, E and Troncoso, P and Ning Tapia, E L and Davis, J W and Titus, M A and Hoang, A and Prokhorova, I N and Wen, S and Logothetis, C                                               | Effects of preoperative abiraterone acetate (AA) plus enzalutamide (E) and leuprolide acetate (LHRHa) versus AA and LHRHa in localized high-risk prostate cancer (LHRPC)                                             | Journal of clinical oncology    | 2015 | 33      | 15     |               | Tipo de publicación equivocada |
| Smith, M R and Matsubara, N and McKay, R R and Piulats, J M and Todenhofer, T and Zhang, T and Fasnacht, N and Sherwood, S and Johnston, E L and Schaverien, C and al., et                  | CYCLONE 3: a phase 3, randomized, double-blind, placebo-controlled study of abemaciclib in combination with abiraterone plus prednisone in men with high-risk, metastatic, hormone-sensitive prostate cancer (mHSPC) | Journal of clinical oncology    | 2023 | 41      | 6      | TPS289-TPS289 | Tipo de publicación equivocada |
| Piulats, J M and Smith, M and Matsubara, N and Zhang, T and Agarwal, N and McKay, R R and Johnston, E and Sherwood, S and Schaverien, C and Fasnacht, N and al., et                         | CYCLONE 3: a Phase 3, randomized, double-blind, placebo-controlled study of abemaciclib in combination with abiraterone plus prednisone in men with high-risk metastatic hormone-sensitive prostate cancer (mHSPC)   | European urology                | 2023 | 83      |        | S757-S757     | Tipo de publicación equivocada |

| Autor                                                                                                                                                                      | Título                                                                                                                                                                                                                                                          | Revista                                                                                                                                                                         | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|---------|--------|-----------|--------------------------------|
| Clarke, N W and Armstrong, A J and Oya, M and Shore, N and Procopio, G and Daniel Guedes, J and Arslan, C and Mehra, N and Parnis, F and Brown, E and al., et              | Efficacy and Safety of Olaparib Plus Abiraterone Versus Placebo Plus Abiraterone in the First-line Treatment of Patients with Asymptomatic/Mildly Symptomatic and Symptomatic Metastatic Castration-resistant Prostate Cancer: analyses from the Phase 3 PROpel | European urology oncology                                                                                                                                                       | 2025 | 8       | 2      | 394-406   | Tratamiento equivocado         |
| Teo, M Y and Taplin, M-E and Eastham, J A and Benoliel, H and Kibel, A S and McBride, S M and Nguyen, P L and Gopalan, A and Lis, R and Scher, H I                         | Metacure: multi-arm multimodality therapy for very high risk localized and low volume metastatic prostatic adenocarcinoma                                                                                                                                       | Journal of clinical oncology                                                                                                                                                    | 2019 | 37      |        |           | Tipo de publicación equivocada |
| Thiery-Vuillemin, A and Saad, F and Armstrong, A J and Oya, M and Vianna, K and Ozguroglu, M and Gedye, C and Buchschacher, G L and Lee, J Y and Emmenegger, U and al., et | Health-related quality of life (HRQoL) and pain outcomes for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) who received abiraterone (abi) and olaparib (ola) versus (vs) abi and placebo (pbo) in the phase III PROpel trial      | Journal of clinical oncology                                                                                                                                                    | 2023 | 41      | 16     | 5012-5012 | Tipo de publicación equivocada |
| Ali, S A and Hoyle, A and James, N D and Parker, C and Brawley, C and Attard, G and Douis, H and Mason, M D and Parmar, M K B and Sydes, M R and al., et                   | Benefit of prostate radiotherapy for patients with lymph node only or < 4 bone metastasis and no visceral metastases: exploratory analyses of metastatic site and number in the STAMPEDE 'M1jRT comparison'                                                     | Annals of oncology                                                                                                                                                              | 2019 | 30      |        | v330-v330 | Tipo de publicación equivocada |
| EUCTR2019-003761-17-IT                                                                                                                                                     | A RANdomized, open label, multicenter study of Docetaxel versus an Androgen Receptor-targeted agent (abiraterone or enzalutamide) as first-line of therapy in mCRPC patients with adverse prognostic factors (RADAR-1 CRPC)                                     | <a href="https://clinicaltrials.gov/ct2/show/study?term=EUCTR2019-003761-17-IT&amp;rank=1">https://clinicaltrials.gov/ct2/show/study?term=EUCTR2019-003761-17-IT&amp;rank=1</a> | 2021 |         |        |           | Tipo de publicación equivocada |
| Saad, F and Armstrong, A J and Ivanescu, C and Bhaduria, H and Ramaswamy, K and Morlock, R and Tombal, B                                                                   | Impact of Enzalutamide (ENZA) on Patient-Reported Outcomes (PROs) in metastatic Hormone-Sensitive Prostate Cancer (mHSPC) patients with no/low urinary symptoms at baseline: results from the ARCHES study                                                      | European urology open science                                                                                                                                                   | 2020 | 19      |        | e867-e868 | Tipo de publicación equivocada |
| Stockler, M R and Hussain, M and Fizazi, K and Saad, F and Rathenborg, P and Shore, N and Demirhan, E and                                                                  | PROSPER: a phase 3, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with non-metastatic castration-resistant prostate cancer (nmCRPC)                                                                                    | Asia-Pacific journal of clinical oncology                                                                                                                                       | 2018 | 14      |        | 53-54     | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                       | Título                                                                                                                                                                                                                                                 | Revista                                                                                                 | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|------|---------|--------|-----------------|--------------------------------|
| Modelska, K and Phung, D and Krivoshik, A and al., et                                                                                                                                       |                                                                                                                                                                                                                                                        |                                                                                                         |      |         |        |                 |                                |
| Fizazi, K and Hussain, M and Saad, F and Shore, N and De Giorgi, U and Efstathiou, E and Ferreira, U and Ivashchenko, P and Madziarska, K and Al-Adhami, M and al., et                      | A phase III, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic (M0) castration-resistant prostate cancer (CRPC): results of PROSPER by age and region                                          | Annals of oncology                                                                                      | 2018 | 29      |        | viii277-viii278 | Tipo de publicación equivocada |
| Chung, B H and McQuarrie, K and Bjartell, A and Chowdhury, S and Pereira De Santana Gomes, A J and Ozguroglu, M and Juarez Soto, A and Merseburger, A S and Uemura, H and Ye, D and al., et | Apalutamide (APA) plus androgen deprivation therapy (ADT) for metastatic castration-sensitive prostate cancer (mCSPC): analysis of pain and fatigue in the TITAN study                                                                                 | Annals of oncology                                                                                      | 2019 | 30      |        | ix68-ix68       | Tipo de publicación equivocada |
| Wang, S and Fu, C and Zou, Q and Li, Y and He, D and Wang, S and Wang, H and Smith, M R and Tombal, B F and Hussain, M H A and al., et                                                      | Efficacy and safety of darolutamide in Chinese patients with metastatic hormone-sensitive prostate cancer (mHSPC): a subpopulation analysis of the phase 3 ARASENS study                                                                               | Journal of clinical oncology                                                                            | 2023 | 41      | 16     | e17076-e17076   | Tipo de publicación equivocada |
| Colomba, E and Jonas, S F and Eymard, J-C and Delva, R and Brachet, P-E and Neuzillet, Y and Penel, N and Roubaud, G and Bompas, E and Mahammedi, H and al., et                             | ODENZA: a French prospective, randomized, open-label, multicenter, cross-over phase II trial of preference between darolutamide and enzalutamide in men with asymptomatic or mildly symptomatic metastatic castration-resistant prostate cancer (CRPC) | Journal of clinical oncology                                                                            | 2021 | 39      | 15     |                 | Tipo de publicación equivocada |
| Hoyle, A P and Ali, A and James, N D and Parker, C C and Cooke, A and Attard, G and Chowdhury, S and Cross, W R and Dearnaley, D P and De Bono, J S and al., et                             | The role of abiraterone acetate plus prednisone/prednisolone in high- and low-risk metastatic hormone sensitive prostate cancer                                                                                                                        | European urology, supplements                                                                           | 2019 | 18      | 1      | e1387-e1388     | Tipo de publicación equivocada |
| Quinn, D I and Tangen, C M and Hussain, M and Lara, P and Goldkorn, A and Garzotto, M and Mack, P C and Carducci, M A and Monk, J P and Twardowski, P and al., et                           | SWOG S0421: phase III study of docetaxel (D) and abiraterone (A) versus docetaxel and placebo (P) for men with advanced castrate resistant prostate cancer (CRPC)                                                                                      | Journal of clinical oncology                                                                            | 2012 | 30      | 15     |                 | Tipo de publicación equivocada |
| EUCTR2008-000701-11-IT                                                                                                                                                                      | A Randomized Double-Blind Phase 3 Trial Comparing Docetaxel Combined with                                                                                                                                                                              | <a href="https://trialssearch.who.int/Trial2.aspx?Tri">https://trialssearch.who.int/Trial2.aspx?Tri</a> | 2008 |         |        |                 | Comparación equivocada         |

| Autor                                                                                                                                                            | Título                                                                                                                                                                                                                                                                                                      | Revista                                                                                                                                                     | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|------|---------|--------|-------------|--------------------------------|
|                                                                                                                                                                  | Dasatinib to Docetaxel Combined with Placebo in Castration-Resistant Prostate Cancer - ND                                                                                                                                                                                                                   | <a href="#">aID=EUCTR2008-000701-11-IT</a>                                                                                                                  |      |         |        |             |                                |
| Aggarwal, R and Eggener, S and Heller, G and Xiao, H and Hillman, D and Picus, J and Wang, J and Taplin, M E and Dorff, T and Appleman, L and al., et            | UPDATED PROGRESSION-FREE SURVIVAL FROM PRESTO: a PHASE 3 RANDOMIZED STUDY OF ANDROGEN ANNIHILATION FOR HIGH-RISK BIOCHEMICALLY RELAPSED PROSTATE CANCER (AFT-19)                                                                                                                                            | Journal of urology                                                                                                                                          | 2023 | 209     |        | e1191-e1191 | Tipo de publicación equivocada |
| NL-OMON55283                                                                                                                                                     | PROCADE: a Multinational Phase 3, Randomized, Double-Blind, Non-Inferiority, Efficacy and Safety Study of Oral HC-1119 versus Enzalutamide in Metastatic Castration-Resistant Prostate Cancer (mCRPC)                                                                                                       | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=NL-OMON55283">https://trialsearch.who.int/Trial2.aspx?TrialID=NL-OMON55283</a>                     | 2019 |         |        |             | Tipo de publicación equivocada |
| EUCTR2004-002203-32-HU                                                                                                                                           | A Multicenter, Open-Label, Randomized, Phase III Trial Comparing Immediate Adjuvant Hormonal Therapy (ELIGARD®-leuprolide acetate) in Combination with TAXOTERE® (docetaxel) Administered Every Three Weeks Versus Hormonal Therapy Alone Versus Deferred Therapy Followed by the Same Therapeutic Optio... |                                                                                                                                                             | 2006 |         |        |             | Tipo de publicación equivocada |
| Morgans, A K and Gschwend, J E and Shore, N D and Ross, A and Feng, F and Hope, T and Trandafir, L and Le Berre, M.-A. and Kuss, I and Joensuu, H and Fizazi, K  | 1841TiP Darolutamide plus androgen-deprivation therapy (ADT) in patients with high-risk biochemical recurrence (BCR) of prostate cancer: A phase III, randomized, double-blind, placebo-controlled study (ARASTEP)                                                                                          | Annals of Oncology                                                                                                                                          | 2023 | 34      |        | S997-S998   | Tipo de publicación equivocada |
| Hamilton, R J and Li, J and Naini, V and Kheoh, T S and Porre, P D and Molina, A and Leibowitz-Amit, R and De Bono, J S and Scher, H I and Ryan, C J and al., et | Effect of concomitant medication use on outcomes of treatment and placebo arms of the COU-AA-301 and COU-AA-302 studies of abiraterone acetate (AA) in metastatic castration-resistant prostate cancer (mCRPC)                                                                                              | Journal of clinical oncology                                                                                                                                | 2014 | 32      | 15     |             | Tipo de publicación equivocada |
| EUCTR2020-003969-19-NL                                                                                                                                           | Open-label study comparing 177Lu-PSMA-617 vs. a change of androgen receptor-directed therapy drugs in the treatment of mCRPC                                                                                                                                                                                | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2020-003969-19-NL">https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2020-003969-19-NL</a> | 2021 |         |        |             | Tipo de publicación equivocada |
| Fizazi, K and Shore, N D and Tammela, T L J and Ulys, A and Vjaters, E and Polyakov, S and Jievahtas, M and Luz, M                                               | Overall survival (OS) results of phase III ARAMIS study of darolutamide (DARO) added to androgen deprivation therapy (ADT) for                                                                                                                                                                              | Annals of oncology                                                                                                                                          | 2020 | 31      |        | S1328-S1328 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                          | Título                                                                                                                                                                                                           | Revista                         | Año  | Volumen | Número | Páginas | Razón de exclusión             |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|------|---------|--------|---------|--------------------------------|
| and Alekseev, B and Kuss, I and al., et                                                                                                                                        | non-metastatic castration-resistant prostate cancer (nmCRPC)                                                                                                                                                     |                                 |      |         |        |         |                                |
| Small, E J and Saad, F and Chowdhury, S and Oudard, S and Hadaschik, B A and Graff, J N and Olmos, D and Mainwaring, P N and Lee, J Y and Uemura, H and al., et                | Final survival results from SPARTAN, a phase III study of apalutamide (APA) versus placebo (PBO) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC)                              | Journal of clinical oncology    | 2020 | 38      | 15     |         | Tipo de publicación equivocada |
| Hadaschik, B A and Small, E J and Saad, F and Chowdhury, S and Graff, J N and Olmos, D and Mainwaring, P N and Uemura, H and Lopez-Gitlitz, A and Trudel, G C and al., et      | SPARTAN, a phase 3 double-blind, randomized study of apalutamide versus placebo in patients with nonmetastatic castration-resistant prostate cancer (nmCRPC)                                                     | Oncology research and treatment | 2018 | 41      |        | 43-43   | Tipo de publicación equivocada |
| Morris, M J and Heller, G and Bryce, A H and Armstrong, A J and Beltran, H and Hahn, O M and McGary, E C and Mehan, P T and Goldkorn, A and Roth, B J and al., et              | Alliance A031201: a phase III trial of enzalutamide (ENZ) versus enzalutamide, abiraterone, and prednisone (ENZ/AAP) for metastatic castration resistant prostate cancer (mCRPC)                                 | Journal of clinical oncology    | 2019 | 37      |        |         | Tipo de publicación equivocada |
| Fizazi, K and Tran, N and Fein, L E and Matsubara, N and Antolin, A R and Alekseev, B Y and Ozguroglu, M and Ye, D and Feyerabend, S and Protheroe, A and al., et              | LATITUDE: a phase III, double-blind, randomized trial of androgen deprivation therapy with abiraterone acetate plus prednisone or placebos in newly diagnosed high-risk metastatic hormone-naïve prostate cancer | Journal of clinical oncology    | 2017 | 35      | 15     |         | Tipo de publicación equivocada |
| Hahn, A W and Wang, X and Efstathiou, E and Hwang, H and Zurita, A J and Spetsieris, N and Boukvala, M A and Wang, J and Araujo, J C and Piliie, P G and al., et               | Third analysis of a randomized trial of finite abiraterone acetate (AA) plus LHRH agonist (LHRHa) versus LHRHa in biochemically recurrent, non-metastatic hormone-naïve prostate cancer (M0HNPC)                 | Journal of clinical oncology    | 2022 | 40      | 6      |         | Tipo de publicación equivocada |
| Ryan, C J and Smith, M R and De Bono, J S and Molina, A and Logothetis, C and De Souza, P L and Fizazi, K and Mainwaring, P N and Piulats Rodriguez, J M and Ng, S and al., et | Interim analysis (IA) results of COU-AA-302, a randomized, phase III study of abiraterone acetate (AA) in chemotherapy-naïve patients (pts) with metastatic castration-resistant prostate cancer (mCRPC)         | Journal of clinical oncology    | 2012 | 30      | 18     |         | Tipo de publicación equivocada |
| Carles, J and Diaz, E G and Domenech, M and Font, A and Bellmunt, J and Mellado, B                                                                                             | A phase IIb trial of docetaxel concurrent with radiotherapy plus hormone therapy versus radio hormone therapy in high-risk localized                                                                             | Journal of clinical oncology    | 2015 | 33      | 7      |         | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                            | Título                                                                                                                                                                                                                                                      | Revista                       | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Tombal, B and Hussain, M and Penson, D and Attard, G and Sternberg, C N and Phung, D and Naidoo, S and Modelska, K and Demirhan, E and Ramaswamy, K and al., et                                  | Patient-reported outcome measures in men with non-metastatic castration-resistant prostate cancer: baseline data from the PROSPER trial                                                                                                                     | European urology, supplements | 2018 | 17      | 2      | e870-e871   | Tipo de publicación equivocada |
| Agarwal, N and McQuarrie, K and Bjartell, A and Chowdhury, S and Pereira De Santana Gomes, A J and Chung, B H and Ozguroglu, M and Juarez Soto, A and Merseburger, A S and Uemura, H and al., et | Patient-reported outcomes (PROs) From TITAN: a phase 3, randomized, double-blind study of apalutamide (APA) versus placebo (PBO) added to androgen deprivation therapy (ADT) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) | European urology, supplements | 2019 | 18      | 11     | e3413-e3414 | Tipo de publicación equivocada |
| Mainwaring, P and Small, E and Saad, F and Chowdhury, S and Oudard, S and Hadaschik, B and Graff, J and Olmos, D and Lee, J and Uemura, H and al., et                                            | Updated analysis of progression-free survival with first subsequent therapy (PFS2) and safety in the SPARTAN study of apalutamide (APA) in patients (pts) with high-risk nonmetastatic castration-resistant prostate cancer (nmCRPC)                        | BJU international             | 2019 | 123     |        | 46-47       | Tipo de publicación equivocada |
| Aggarwal, R R and Alumkal, J J and Szmulewitz, R Z and Higano, C S and Bryce, A H and Lopez-Gitlitz, A and McCarthy, S A and Miladinovic, B and McQuarrie, K and Thomas, S and al., et           | A randomized phase II study of apalutamide (APA), androgen deprivation therapy (ADT), or APA + ADT in patients (pts) with biochemically relapsed (BCR) prostate cancer (PC)                                                                                 | Journal of clinical oncology  | 2020 | 38      | 6      |             | Tipo de publicación equivocada |
| Saad, F and Vjaters, E and Shore, N D and Olmos, D and Xing, N and Gomes, AJPDS and Mota, A C A and Salman, P and Jievaltas, M and Ulys, A and al., et                                           | LBA68 Efficacy and safety of darolutamide plus androgen-deprivation therapy (ADT) in patients with metastatic hormone-sensitive prostate cancer (mHSPC) from the phase III ARANOTE trial                                                                    | Annals of oncology            | 2024 | 35      |        | S1257-S1258 | Tipo de publicación equivocada |
| Armstrong, A and Tombal, B and Saad, F and Parli, T and Phung, D and Beer, T M                                                                                                                   | Enzalutamide in men with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC): long-term overall survival and safety analyses of the phase 3 PREVAIL study                                                                            | European urology, supplements | 2019 | 18      | 1      | e1217-e1218 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                           | Título                                                                                                                                                                                                                                                                   | Revista                                                                                                                                                   | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| Chi, K N and Tran, N and Feyerabend, S and Matsubara, N and Ozguroglu, M and Fein, L E and Antolin, A R and Alekseev, B Y and Sulur, G and Protheroe, A and al., et             | Subsequent treatment after abiraterone acetate + prednisone (AA + P) in patients (pts) with newly diagnosed high-risk metastatic castration-naïve prostate cancer (NDx-HR mCNPc): detailed analyses from the phase 3 LATITUDE trial                                      | Journal of clinical oncology                                                                                                                              | 2018 | 36      | 15     |         | Tipo de publicación equivocada |
| Khalaf, D and Annala, M and Finch, D L and Oja, C D and Vergidis, J and Zulfiqar, M and Sunderland, K and Beja, K and Vandekerckhove, G R and Gleave, M and al., et             | Phase 2 randomized cross-over trial of abiraterone + prednisone (ABI+P) vs enzalutamide (ENZ) for patients (pts) with metastatic castration resistant prostate cancer (mCPRC): results for 2nd-line therapy                                                              | Journal of clinical oncology                                                                                                                              | 2018 | 36      | 15     |         | Tipo de publicación equivocada |
| Tombal, B F and Lortot, Y and Saad, F and McDermott, R S and Marreaud, S and Collette, L and Gillesen, S                                                                        | Intergroup study EORTC-1333-GUCCG: a randomized multicenter phase III trial comparing enzalutamide vs. a combination of Ra223 and enzalutamide in asymptomatic or mildly symptomatic castration resistant prostate cancer (CRPC) patients metastatic to bone (PEACE III) |                                                                                                                                                           | 2018 | 36      | 6      |         | Tipo de publicación equivocada |
| Yijun, S and Dingwei, Y                                                                                                                                                         | Docetaxel plus prednisone versus mitoxantrone plus prednisone as firstline chemotherapy for metastatic castration-refractory prostate cancer: long-term effects and safety in chinese                                                                                    | International journal of urology                                                                                                                          | 2012 | 19      |        | 155-155 | Tipo de publicación equivocada |
| Van Poppel, H and Rathkopf, D and Smith, M R and De Bono, J S and Logothetis, C J and Shore, N D and De Souza, P and Fizazi, K and Mulders, P F A and Mainwaring, P and al., et | Updated interim analysis (IA): results of randomized phase 3 study COUAA-302 of abiraterone acetate (AA) in metastatic castration-resistant prostate cancer (mCRPC) patients (pts) without prior chemotherapy                                                            | European urology, supplements                                                                                                                             | 2013 | 12      | 1      | e97-e98 | Tipo de publicación equivocada |
| Maluf, F C and Soares, A and Bastos, D A and Schutz, F A B and Cronemberger, E and Luz, M and Martins, S P S and Muniz, D Q B and Carcano, F M and Smaletz, O and al., et       | Survival analysis of the randomized phase II trial to investigate androgen signaling inhibitors with or without androgen deprivation therapy (ADT) for castration-sensitive prostate cancer: LACOG 0415                                                                  | Journal of clinical oncology                                                                                                                              | 2022 | 40      | 16     |         | Tipo de publicación equivocada |
| CTIS2023-505852-23-00                                                                                                                                                           | Apalutamide, Radiotherapy and LHRH Agonist in High-Risk Hormone-Sensitive Prostate Cancer Patients Assessed by PSMA-PET                                                                                                                                                  | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=CTIS2023-505852-23-00">https://trialsearch.who.int/Trial2.aspx?TrialID=CTIS2023-505852-23-00</a> | 2024 |         |        |         | Tipo de publicación equivocada |



| Autor                                                                                                                                                                              | Título                                                                                                                                                                                                                                                          | Revista                                                     | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Hadaschik, B A and Smith, M R and Saad, F and Chowdhury, S and Oudard, S and Graff, J N and Olmos, D and Mainwaring, P N and Lee, J Y and Uemura, H and al., et                    | Apalutamide (APA) and overall survival (OS) in patients (PTS) with nonmetastatic castration-resistant prostate cancer (NMCRPC): updated results from the phase 3 spartan study                                                                                  | Oncology research and treatment                             | 2020 | 43      |        | 71-71       | Tipo de publicación equivocada |
| Chiong, E and Kim, C S and Choi, Y D and Tombal, B and Lian, M and Gourgioti, G and Dhar, A and Xiao, Z and Zohren, F and Beer, T                                                  | Association of enzalutamide (ENZA) duration of treatment (DOT) and overall survival (OS) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC): post hoc analysis from PREVAIL                                                         | Annals of oncology                                          | 2023 | 34      |        | S1573-S1573 | Tipo de publicación equivocada |
|                                                                                                                                                                                    | Docetaxel Plus 6-month Androgen Suppression and Radiation Therapy Versus 6-month Androgen Suppression and Radiation Therapy for Patients With High Risk Localized or Locally Advanced Prostate Cancer: A Randomized Controlled Trial                            | <a href="https://clinicaltrials.gov">clinicaltrials.gov</a> | 2005 |         |        |             | Tipo de publicación equivocada |
| Tagawa, S T and Armstrong, A J and Krause, B J and Herrmann, K and Rahbar, K and De Bono, J S and Adra, N and Desilvio, M and Messmann, R and Holder, G and al., et                | Tolerability of [177Lu]Lu-PSMA-617 by treatment exposure in patients with metastatic castration-resistant prostate cancer (mCRPC): a VISION study subgroup analysis                                                                                             | Journal of clinical oncology                                | 2022 | 40      | 16     |             | Tipo de publicación equivocada |
| Kim, H and Tagawa, S T and Sartor, A O and Saad, F and Reid, A and Sakharova, O and Feng, F Y and Fizazi, K and Morris, M                                                          | PSMAAddition: phase 3 Trial of [177Lu]Lu-PSMA-617 Plus Standard of Care (SoC) vs. Soc Alone in Patients with Metastatic Hormone-Sensitive Prostate Cancer                                                                                                       | International journal of radiation oncology biology physics | 2024 | 120     | 2      | e546-e546   | Tipo de publicación equivocada |
| Sandler, H M and Freedland, S J and Shore, N D and Smith, M R and Rosales, R S and Brookman-May, S D and Dearnaley, D P and Dicker, A P and McKenzie, M R and Bossi, A and al., et | Patient (pt) population and radiation therapy (RT) type in the long-term phase 3 double-blind, placebo (PBO)-controlled ATLAS study of apalutamide (APA) added to androgen deprivation therapy (ADT) in high-risk localized or locally advanced prostate cancer | Journal of clinical oncology                                | 2022 | 40      | 16     |             | Tipo de publicación equivocada |
| Sartor, O and Castellano Gauna, D E and Herrmann, K and de Bono, J S and Shore, N D and Chi, K N N and Crosby, M and Piulats Rodriguez, J M                                        | LBA13 Phase III trial of [177Lu]Lu-PSMA-617 in taxane-naïve patients with metastatic castration-resistant prostate cancer (PSMAfore)                                                                                                                            | Annals of oncology                                          | 2023 | 34      |        | S1324-S1325 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                                                                                 | Título                                                                                                                                                                                                                   | Revista                      | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
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| Patrick-Miller, L J and Chen, Y-H and Carducci, M A and Cella, D and DiPaola, R S and Gartrell, B A and Liu, G and Jarrard, D F and Morgans, A K and Wong, Y-N and al., et                                                                                                                                                                                            | Quality of life (QOL) analysis from CHAARTED: chemohormonal androgen ablation randomized trial in prostate cancer (E3805)                                                                                                | Journal of clinical oncology | 2016 | 34      |        |                 | Tipo de publicación equivocada |
| Hu, Z and Ye, Z and Zeng, H and Huang, Y and Ye, D and Shi, B and Luo, H and Du, C and An, W and Zhou, L and al., et                                                                                                                                                                                                                                                  | Abiraterone acetate in men with metastatic castration-resistant prostate cancer and no prior chemotherapy: a double-arm, multiple-centre, phase III clinical study                                                       | Annals of oncology           | 2020 | 31      |        | S530-S530       | Tipo de publicación equivocada |
| Tombal, B and Hussain, M and Penson, D and Attard, G and Sternberg, C N and Phung, D and Morlock, R and Modelska, K and Ramaswamy, K and Ivanescu, C and al., et                                                                                                                                                                                                      | Prolonged urinary and bowel symptom control in men with nonmetastatic castration-resistant prostate cancer (nmCRPC) treated with enzalutamide: results from the PROSPER study                                            | Annals of oncology           | 2018 | 29      |        | viii278-viii279 | Tipo de publicación equivocada |
| Soares, A and Bastos, D A and Schutz, F A B and Cronemberger, E and Luz, M and Martins, S P S and Muniz, D Q B and Carcano, F M and Smaletz, O and Peixoto, F A and al., et                                                                                                                                                                                           | Health-related quality-of-life (HRQoL) analysis from a randomized phase II trial of androgen signaling inhibitors with or without androgen deprivation therapy (ADT) for castrationsensitive prostate cancer: LACOG 0415 | Journal of clinical oncology | 2021 | 39      | 6      |                 | Tipo de publicación equivocada |
| Vale, C L and Fisher, D J and Godolphin, P J and Rydzewska, L H and Boher, J.-M. and Burdett, S and Chen, Y.-H. and Clarke, N W and Fizazi, K and Gravis, G and James, N D and Liu, G and Matheson, D and Murphy, L and Oldroyd, R E and Parmar, M K B and Rogozinska, E and Sfumato, P and Sweeney, C J and Sydes, M R and Tombal, B and White, I R and Tierney, J F | Which patients with metastatic hormone-sensitive prostate cancer benefit from docetaxel: a systematic review and meta-analysis of individual participant data from randomised trials                                     | The Lancet Oncology          | 2023 | 24      | 7      | 783-797         | Tratamiento equivocado         |

| Autor                                                                                                                                                                             | Título                                                                                                                                                                                                                                               | Revista                                                                 | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Freedland, S J and Gleave, M E and De Giorgi, U F F and Rannikko, A and Pieczonka, C and Tutrone, R and Venugopal, B and Woo, H and Ramirez Backhaus, M and Supiot, S and al., et | 1766MO Health-related quality of life (HRQoL) in nonmetastatic hormone-sensitive prostate cancer (nmHSPC) patients (pts) with high-risk biochemical recurrence (BCR) from the EMBARK study                                                           | Annals of oncology                                                      | 2023 | 34      |        | S955-S955 | Tipo de publicación equivocada |
| Oudard, S and Hadaschik, B A and Saad, F and Cella, D and Basch, E and Mainwaring, P N and Graff, J N and Dibaj, S and Li, S and Brookman-May, S D and al., et                    | Health-related quality of life (HRQoL) at final analysis of the SPARTAN study of apalutamide (APA) vs placebo (PBO) in patients (pts) with non-metastatic castration-resistant prostate cancer (nmCRPC) receiving androgen deprivation therapy (ADT) | Annals of oncology                                                      | 2020 | 31      |        | S521-S521 | Tipo de publicación equivocada |
| James, N and De Bono, J and Spears, M R and Clarke, N W and Mason, M D and Dearnaley, D and Ritchie, A W S and Russell, M and Gilson, C and Jones, R and al., et                  | Adding abiraterone for patients (pts) with high-risk prostate cancer (PCa) starting long-term androgen deprivation therapy (ADT): outcomes in non-metastatic (M0) patients from STAMPEDE (NCT00268476)                                               | Annals of oncology                                                      | 2017 | 28      |        | v620-v620 | Tipo de publicación equivocada |
| Jiang, S and Terasawa, E and Horton, V G and Ayyagari, R and Waldeck, A R and Halabi, S and Shore, N D                                                                            | Safety outcomes of darolutamide versus apalutamide and enzalutamide in nonmetastatic castration-resistant prostate cancer (nmCRPC): matchingadjusted indirect comparisons                                                                            | Journal of clinical oncology                                            | 2020 | 38      | 15     |           | Tipo de publicación equivocada |
| Eisenberger, M A and De Wit, R and Berry, W and Bodrogi, I and Pluzanska, A and Chi, K and Oudard, S and Christine, T and James, N and Tannock, I                                 | A multicenter phase III comparison of docetaxel (D) + prednisolon (P) and mitoxantrone (MTZ) + P in patients with hormone-refractory prostate cancer (HRPC)                                                                                          | Annual meeting proceedings of the american society of clinical oncology |      |         |        | 2-2       | Tipo de publicación equivocada |
| Feyerabend, S and Tran, N and Fein, L and Matsubara, N and Rodriguez Antolin, A and Alekseev, B and Ozguroglu, M and Ye, D and Protheroe, A and De Porre, P and al., et           | LATITUDE, a phase 3 double-blind, randomized trial of androgen deprivation therapy (ADT) with abiraterone acetate (AA) plus prednisone (P) or placebos (PBOs) in patients (pts) with newly diagnosed high-risk                                       | Oncology research and treatment                                         | 2017 | 40      |        | 113-113   | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                      | Título                                                                                                                                                                                                                     | Revista                                   | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| De Souza, P and Smith, M R and De Bono, J S and Molina, A and Logothetis, C and Fizazi, K and Piulats, J M and Ng, S and Carles, J and Mulders, P F A and al., et                                          | Abiraterone acetate (AA) in chemotherapy-naïve patients with metastatic castration-resistant prostate cancer (MCRPC): results of interim analysis (IA) of COU-AA-302, a randomized phase 3 study                           | Asia-Pacific journal of clinical oncology | 2012 | 8       |        | 163-163     | Tipo de publicación equivocada |
| Aggarwal, R and Heller, G and Hillman, D and Xiao, H and Picus, J and Wang, J and Taplin, M E and Dorff, T and Appleman, L J and Weckstein, D and al., et                                                  | LBA63 PRESTO: a phase III, open-label study of androgen annihilation in patients (pts) with high-risk biochemically relapsed prostate cancer (AFT-19)                                                                      | Annals of oncology                        | 2022 | 33      |        | S1428-S1428 | Tipo de publicación equivocada |
| Tan, T and Smith, M R and Fred, S and Chowdhury, S and Oudard, S and Hadaschik, B A and Graff, J N and Olmos, D and Mainwaring, P N and Lee, J Y and al., et                                               | Apalutamide and overall survival in patients with nonmetastatic castration-resistant prostate cancer: updated results from the phase 3 SPARTAN study                                                                       | Asia-Pacific journal of clinical oncology | 2019 | 15      |        | 123-123     | Tipo de publicación equivocada |
| Fizazi, K and Shore, N D and Tammela, T and Ulys, A and Vjaters, E and Polyakov, S and Jievaltas, M and Luz, M and Alekseev, B Y and Kuss, I and Kappeler, C and Snapir, A and Sarapohja, T and Smith, M R | ARAMIS: Efficacy and safety of darolutamide in non-metastatic castration-resistant prostate cancer (nmCRPC)                                                                                                                | Journal of Clinical Oncology              | 2019 | 37      |        |             | Tipo de publicación equivocada |
| Glode, L M and Tangen, C M and Hussain, M and Swanson, G P and Wood, D P and Sakr, W and Dawson, N A and Haas, N B and Flaig, T W and Dorfi, T B and al., et                                               | Adjuvant androgen deprivation (ADT) versus mitoxantrone plus prednisone (MP) plus ADT in high-risk prostate cancer (PCa) patients following radical prostatectomy: a phase III intergroup trial (SWOG S9921) NCT00004124   | Journal of clinical oncology              | 2017 | 35      | 6      |             | Tipo de publicación equivocada |
| Shore, N and Basch, E and Ryan, C J and Mulders, P and Kheoh, T and Fizazi, K and Logothetis, C J and Rathkopf, D and Smith, M R and Mainwaring, P N and al., et                                           | The impact of abiraterone acetate therapy on patient-reported pain and functional status in chemotherapy-naïve patients with progressive, metastatic castration-resistant prostate cancer-results from an updated analysis | Journal of urology                        | 2013 | 189     | 4      | e323-e323   | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                          | Título                                                                                                                                                                                                                | Revista                                                                                                                                                     | Año  | Volumen | Número | Páginas       | Razón de exclusión             |
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| Sargos, P and Mottet, N and Molinie, V and Richaud, P M                                                                                                                                                                                                        | Long-term androgen deprivation, with or without radiation therapy, in locally advanced prostate cancer: results from a phase 3 randomized study after 7.3 years' median follow-up                                     | International journal of radiation oncology                                                                                                                 | 2016 | 96      | 2      | S138-S139     | Tipo de publicación equivocada |
| Merseburger, A S and Agarwal, N and Bhaumik, A and Lefresne, F and Karsh, L I and Pereira de Santana Gomes, A J and Soto, A J and Given, R W and Brookman-May, S D and Mundle, S D and al., et                                                                 | Apalutamide plus androgen deprivation therapy in clinical subgroups of patients with metastatic castration-sensitive prostate cancer: a subgroup analysis of the randomised clinical TITAN study                      | European journal of cancer (Oxford, England : 1990)                                                                                                         | 2023 | 193     |        | 113290-113290 | Tipo de publicación equivocada |
| EUCTR2017-000155-21-FR                                                                                                                                                                                                                                         | An open label, randomized, phase III study, evaluating the efficacy of a Combination of Apalutamide with Radiotherapy and LHRH Agonist in high-risk postprostatectomy biochemically relapsed prostate cancer patients | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2017-000155-21-FR">https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2017-000155-21-FR</a> | 2019 |         |        |               | Tipo de publicación equivocada |
| De Souza, P and Rathkopf, D and Smith, M and Mulders, P and Mainwaring, P and North, S and Griffin, T and Park, Y and Molina, A and Ryan, C                                                                                                                    | Long-term safety and efficacy analysis of abiraterone acetate (AA) plus prednisone (P) in study COU-AA-302 for metastatic castration-resistant prostate cancer                                                        | BJU international                                                                                                                                           | 2013 | 112     |        | 13-13         | Tipo de publicación equivocada |
| Yanagisawa, T and Rajwa, P and Thibault, C and Gandaglia, G and Mori, K and Kawada, T and Fukuokaya, W and Shim, S R and Mostafaei, H and Motlagh, R S and Quhal, F and Laukhtina, E and Pallauf, M and Pradere, B and Kimura, T and Egawa, S and Shariat, S F | Androgen Receptor Signaling Inhibitors in Addition to Docetaxel with Androgen Deprivation Therapy for Metastatic Hormone-sensitive Prostate Cancer: A Systematic Review and Meta-analysis                             | European Urology                                                                                                                                            | 2022 | 82      | 6      | 584-598       | Tratamiento equivocado         |
|                                                                                                                                                                                                                                                                | LBA02-09 EMBARK: a Phase 3 Randomized Study of Enzalutamide or Placebo Plus Leuprolide Acetate and Enzalutamide Monotherapy in High-risk Biochemically Recurrent Prostate Cancer                                      | Journal of urology                                                                                                                                          | 2023 | 210     | 1      | 224-226       | Tipo de publicación equivocada |
| Baciarello, G and Ozguroglu, M and Mundle, S D and Leitz,                                                                                                                                                                                                      | Impact of abiraterone acetate plus prednisone (AAP) in patients with castration-sensitive prostate cancer (mCSPC) and                                                                                                 | Annals of oncology                                                                                                                                          | 2020 | 31      |        | S530-S531     | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                                                          | Título                                                                                                                                                                                                                                            | Revista                             | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
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| G and Richarz, U and Hu, P and Chi, K N and Fizazi, K                                                                                                                                                                                                                                                                                          | visceral metastases: subgroup analyses of the LATITUDE study                                                                                                                                                                                      |                                     |      |         |        |                 |                                |
| SJ, Freedland and U, De Giorgi and M, Gleave and B, Rosbrook and Q, Shen and J, Sugg and GP, Haas and ND, Shore                                                                                                                                                                                                                                | A phase 3 randomised study of enzalutamide plus leuprolide and enzalutamide monotherapy in high-risk non-metastatic hormone-sensitive prostate cancer with rising PSA after local therapy: EMBARK study design.                                   | BMJ open                            | 2021 | 11      | 8      | e046588-e046588 | Tipo de publicación equivocada |
| Steuber, T and Heinzer, H and Haese, A and Strolin, P and Parker, C and Coleman, R E and Nilsson, S and Vogelzang, N and Loyd, A J and Staudacher, K and al., et                                                                                                                                                                               | Updated Survival, Quality of life (QOL) and Safety-data of Radium223 Dichlorid (Ra223) in patients with castration resistant prostate cancer (CRPC) with bone metastasis from the Phase 3 double-blind randomised, multinational study (ALSYMPCA) | Onkologie                           | 2013 | 36      |        | 17-17           | Tipo de publicación equivocada |
| James, N and Rush, H and Clarke, N and Attard, G and Cook, A and Dearnaley, D and Gillessen, S and Hoyle, A and Jones, R and Millman, R and Birtle, A and Chowdhury, S and Gale, J and Malik, Z and O'Sullivan, J and Pezaro, C and Sheehan, D and Tanguay, J and Parmar, M K and Sydes, M R                                                   | Abiraterone acetate plus prednisolone for hormone-naïve prostate cancer (PCA): Long-term results from metastatic (M1) patients in the STAMPEDE randomised trial (NCT00268476)                                                                     | Annals of Oncology                  | 2020 | 31      |        | S509-S509       | Tipo de publicación equivocada |
| M, Uemura and H, Kikukawa and Y, Hashimoto and H, Uemura and A, Mizokami and M, Kato and H, Matsushima and T, Kosaka and M, Nakamura and S, Fukasawa and MR, Smith and B, Tombal and M, Hussain and F, Saad and K, Fizazi and CN, Sternberg and ED, Crawford and H, Kakiuchi and M, Akiyama and R, Li and I, Kuss and H, Joensuu and H, Suzuki | Darolutamide in Japanese patients with metastatic hormone-sensitive prostate cancer: Phase 3 ARASENS subgroup analysis.                                                                                                                           | Cancer medicine                     | 2024 | 13      | 21     | e70029-e70029   | Tipo de publicación equivocada |
| Z, Zhou and S, Liu and J, Mei and T, Liu and F, Liu and G, Zhang                                                                                                                                                                                                                                                                               | Systemic therapies for high-volume metastatic hormone-sensitive prostate cancer: a network meta-analysis.                                                                                                                                         | Acta oncologica (Stockholm, Sweden) | 2023 | 62      | 9      | 1083-1090       | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                     | Título                                                                                                                                                                                                                                                          | Revista                             | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Shore, N and Stenzl, A and Pieczonka, C and Klaassen, Z and Aronson, W and Karsh, L and Ryan, C and Miskic, M and Srinivasan, S and Mohamed, A and al., et                                                                | Impact of darolutamide on local symptoms in patients with nonmetastatic castration-resistant prostate cancer                                                                                                                                                    | Journal of urology                  | 2021 | 206     |        | e586-e587 | Tipo de publicación equivocada |
| Feyerabend, S and Shore, N and Smith, M and Kopyltsov, E and Antonyan, I and Damber, J-E and Gasparro, D and Yildirim, A and Hellstrom, M and Vjaters, E and al., et                                                      | Clinical benefit and safety profile of darolutamide in patients who crossed over to darolutamide from placebo during the open-label period of the phase 3 ARAMIS study                                                                                          | Oncology research and treatment     | 2021 | 44      |        | 265-265   | Tipo de publicación equivocada |
| W, Baccaglini and AF, Rodrigues and SB, Teles and NM, Christofe and FPA, Glina and GC, Lemos and R, Sanchez-Salas and R, Olivares and A, Carneiro                                                                         | The current role of local treatment in metastatic prostate cancer: systematic review and meta-analysis.                                                                                                                                                         | Acta oncologica (Stockholm, Sweden) | 2022 | 61      | 11     | 1386-1393 | Comparación equivocada         |
| Jian, T and Zhan, Y and Hu, K and He, L and Chen, S and Hu, R and Lu, J                                                                                                                                                   | Systemic triplet therapy for metastatic hormone-sensitive prostate cancer: A systematic review and network meta-analysis                                                                                                                                        | Frontiers in Pharmacology           | 2022 | 13      |        |           | Tratamiento equivocado         |
| Ohlmann, C H and Ruessel, C and Zillmann, R and Hellmis, E and Suttman, H and Janssen, M and Marin, J and Dahm, J and Hubner, A and Gleissner, J and al., et                                                              | Abiraterone acetate plus prednisone (AA+P) without continuing LHRH-therapy in patients with metastatic chemotherapy: naive castrations-resistant prostate cancer-Results from the SPARE-trial (NCT02077634)                                                     | Journal of clinical oncology        | 2019 | 37      |        |           | Tipo de publicación equivocada |
| Rathkopf, D E and Efstathiou, E and Attard, G and Flaig, T W and Franke, F A and Goodman, O B and Oudard, S and Steuber, T and Suzuki, H and Wu, D and Yervu, K and De Porre, P and Brookman-May, S D and Li, S and Li, J | Final results from ACIS, a randomized, placebo (PBO)- controlled double-blind phase 3 study of apalutamide (APA) and abiraterone acetate plus prednisone (AAP) versus AAP in patients (pts) with chemo-naive metastatic castration-resistant prostate cancer (m | Journal of Clinical Oncology        | 2021 | 39      | 6      |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                     | Título                                                                                                                                                                                                                                  | Revista                                                                                                                                                   | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
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| Sweeney, C and Chen, Y-H and Carducci, M A and Liu, G and Jarrard, D F and Eisenberger, M A and Wong, Y-N and Hahn, N M and Kohli, M and Vogelzang, N J and al., et       | Impact on overall survival (OS) with chemohormonal therapy versus hormonal therapy for hormone-sensitive newly metastatic prostate cancer (MPRCA): an ECOG-led phase iii randomized trial                                               | Journal of clinical oncology                                                                                                                              | 2014 | 32      | 18     |                 | Tipo de publicación equivocada |
| Francolini, G and Di Cataldo, V and Garlatti, P and Caini, S and Bruni, A and Simoni, N and Augugliaro, M and Iacovelli, R and Tagliaferri, L and Battelli, N and al., et | PERSIAN trial: early results from a randomized phase II trial testing apalutamide and stereotactic body radiation therapy for low-burden, metastatic, hormonesensitive prostate cancer                                                  | Journal of clinical oncology                                                                                                                              | 2025 | 43      |        |                 | Tipo de publicación equivocada |
| CTIS2023-509221-47-00                                                                                                                                                     | A Clinical study to assess the safety and effectiveness of ARN-509 in men with Castration-Resistant Prostate Cancer (prostate cancer not responsive to castration treatment)                                                            | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=CTIS2023-509221-47-00">https://trialsearch.who.int/Trial2.aspx?TrialID=CTIS2023-509221-47-00</a> | 2024 |         |        |                 | Tipo de publicación equivocada |
| Siemens, D R and Heidenreich, A and Klotz, L and Villers, A and Van Os, S and Phung, D and Wang, F and Forer, D and Chowdhury, S and Shore, N                             | A Randomized, Double-blind, Phase 2 Efficacy And Safety Study Of Enzalutamide Versus Bicalutamide In Metastatic Castrationresistant Prostate Cancer: the TERRAIN Trial                                                                  | Canadian urological association journal                                                                                                                   | 2015 | 9       | 9      | S208-S208       | Tipo de publicación equivocada |
| Guadalupi, V and Rametta, A and Verzoni, E and Claps, M and Sepe, P and Stellato, M and Bottiglieri, A and Catanzaro, M and Avuzzi, B and Sighinolfi, M C and al., et     | APPROACH trial: multimodal approach in patients with mHSPC: a pragmatic, randomized, phase 3 trial of androgen-deprivation therapy (ADT) plus apalutamide (APA) versus ADT plus apalutamide (APA) and local treatment Meet-URO 29 study | Journal of clinical oncology                                                                                                                              | 2023 | 41      | 16     | TPS5115-TPS5115 | Tipo de publicación equivocada |
| Chung, B H and Huang, J and Uemura, H and Choi, Y D and Ye, Z and Suzuki, H and Kang, T W and He, D and Joung, J Y                                                        | Apalutamide (APA) efficacy and safety in Asian patients with metastatic castration-sensitive prostate cancer (mCSPC)                                                                                                                    | Annals of oncology                                                                                                                                        | 2021 | 32      |        | S649-S650       | Tipo de publicación equivocada |



| Autor                                                                                                                                                                         | Título                                                                                                                                                                                                                                                  | Revista                      | Año  | Volumen | Número | Páginas                 | Razón de exclusión             |
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| Lledo, D S and Chu, X and Jarrard, D F and Carducci, M A and DiPaola, R S and Wagner, L I and Cella, D and Sweeney, C and Morgans, A K                                        | Patient reported quality of life (QOL) and survival outcomes: analysis of ECOG-ACRIN E3805 chemohormonal androgen ablation randomized trial (CHAARTED) in prostate cancer (PCa)                                                                         | Journal of clinical oncology | 2023 | 41      | 16     | 5014-5014               | Tipo de publicación equivocada |
| Beer, T M and Armstrong, A J and Sternberg, C N and Higano, C S and Iversen, P and Lortot, Y and Rathkopf, D E and Bhattacharya, S and Carles, J and De Bono, J S and al., et | Enzalutamide in men with chemotherapy-naïve metastatic prostate cancer (mCRPC): results of phase III PREVAIL study                                                                                                                                      | Journal of clinical oncology | 2014 | 32      | 4      |                         | Tipo de publicación equivocada |
| Maiorano, B A and De Giorgi, U and Roviello, G and Messina, C and Altavilla, A and Cattrini, C and Mennitto, A and Maiello, E and Di Maio, M                                  | Addition of androgen receptor targeted agents to androgen deprivation therapy and docetaxel in metastatic hormone-sensitive prostate cancer: a systematic review and meta-analysis                                                                      | ESMO Open                    | 2022 | 7       | 5      |                         | Tratamiento equivocado         |
| Warli, S M and Velaro, A J and Firsty, N N and Tala, Z Z                                                                                                                      | Addition of Olaparib to the New Hormonal Agent Regimen for Metastatic Castration-Resistant Prostate Cancer: A Systematic Review and Meta-Analysis                                                                                                       | World Journal of Oncology    | 2023 | 14      | 6      | 518-528                 | Tratamiento equivocado         |
| Boccon-Gibod, L and Fournier, G and Bottet, P and Marechal, J M and Guiter, J and Rischman, P and Hubert, J and Soret, J Y and Mangin, P and Mallo, C and al., et             | Flutamide versus orchidectomy in the treatment of metastatic prostate carcinoma                                                                                                                                                                         | European urology             | 1997 | 32      | 4      | 391-5; discussion 395-6 | Tratamiento equivocado         |
| Fiorica, F and Buttiglieri, C and Grigolato, D and Muraro, M and Turco, F and Munoz, F and Tucci, M                                                                           | Addition of New Androgen Receptor Pathway Inhibitors to Docetaxel and Androgen Deprivation Therapy in Metastatic Hormone-Sensitive Prostate Cancer: A Systematic Review and Metanalysis                                                                 | Current Oncology             | 2022 | 29      | 12     | 9511-9524               | Tratamiento equivocado         |
| Fizazi, K and Tran, N and Enrique Fein, L and Matsubara, N and Antolin, A R and Ozguroglu, M and Ye, D and Feyerabend, S and Protheroe, A and Sulur, G and al., et            | Final analysis of phase III LATITUDE study in patients (pts) with newly diagnosed high-risk metastatic castration-naïve prostate cancer (NDx-HR mCNPC) treated with abiraterone acetate + prednisone (AA+P) added to androgen deprivation therapy (ADT) | Journal of clinical oncology | 2019 | 37      |        |                         | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                         | Título                                                                                                                                                                            | Revista                                     | Año  | Volumen | Número | Páginas             | Razón de exclusión             |
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| Mainwaring, P and Small, E and Uemura, H and Lee, J Y and Pang, S-T and Marx, G and Kwon, T G and Satoh, T and Bhaumik, A and Cheng, S                                                                                                        | Efficacy and safety of apalutamide (APA) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC) from SPARTAN: asian subpopulation                     | Annals of oncology                          | 2018 | 29      |        |                     | Tipo de publicación equivocada |
| Ozguroglu, M and Chowdhury, S and Bjartell, A and Uemura, H and Chung, B H and Agarwal, N and Merseburger, A S and Soto, A J and Lopez-Gitlitz, A and Bhaumik, A and al., et                                                                  | Apalutamide (APA) for metastatic castration-sensitive prostate cancer (mCSPC) in TITAN: outcomes in patients (pts) with low- and high-risk disease                                | Journal of clinical oncology                | 2020 | 38      | 6      |                     | Tipo de publicación equivocada |
| Mulders, P and Fizazi, K and Saad, F and Sternberg, C N and Taplin, M and Miller, K and Chi, K N and Armstrong, A J and Basch, E M and Heidenreich, A and al., et                                                                             | Enzalutamide, an androgen receptor signaling inhibitor, improves overall survival, time to first skeletal related event and pain                                                  | European urology, supplements               | 2012 | 11      | 5      | 188-189             | Tipo de publicación equivocada |
| NJ, Sathianathen and MC, Oestreich and SJ, Brown and S, Gupta and BR, Konety and P, Dahm and F, Kunath                                                                                                                                        | Abiraterone acetate in combination with androgen deprivation therapy compared to androgen deprivation therapy only for metastatic hormone-sensitive prostate cancer.              | The Cochrane database of systematic reviews | 2020 | 12      | 12     | CD013245 - CD013245 | Tipo de publicación equivocada |
| Faure, N and Lemay, A and Laroche, B and Robert, G and Plante, R and Jean, C and Thabet, M and Roy, R and Fazekas, A T A                                                                                                                      | Preliminary results on the clinical efficacy and safety of androgen inhibition by an LHRH agonist alone or combined with an antiandrogen in the treatment of prostatic carcinoma  | The Prostate                                | 1983 | 4       | 6      | 601-624             | Tratamiento equivocado         |
| Roy, S and Malone, S and Wing, K and Chowdhury, S and Kishan, A U and Sun, Y and Wallis, C J D and Mohamad, O and Jia, A Y and Swami, U and Zaorsky, N G and Morgan, S C and Ong, M and Agarwal, N and Spratt, D E and Small, E J and Saad, F | Prior Local Therapy and First-Line Apalutamide in Patients with Nonmetastatic Castration-Resistant Prostate Cancer: A Secondary Analysis of the SPARTAN Randomized Clinical Trial | JAMA Network Open                           | 2024 | 7       | 10     | e2439434-e2439434   | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                           | Título                                                                                                                                                                                                                                          | Revista                                                                                                                                               | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| CTRI/2018/07/014703                                                                                                                                                                                                             | Comparison of therapeutic efficacy between two different treatment methods in patients with prostate cancer                                                                                                                                     | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2018/07/014703">https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2018/07/014703</a> | 2018 |         |        |             | Tipo de publicación equivocada |
| Sweeney, C and Chen, Y and Carducci, M and Liu, G and Jarrard, D and Eisenberger, M and Wong, Y and Hahn, N M and Kohli, M and Vogelzang, N and al., et                                                                         | Chemohormonal Therapy Versus Hormonal Therapy for Hormone Naïve High Volume Newly Metastatic Prostate Cancer (Prca): ecog Led Phase III Randomized Trial                                                                                        | Annals of oncology                                                                                                                                    | 2014 | 25      |        | iv256-iv256 | Tipo de publicación equivocada |
| Schlack, K and Smith, M R and Shore, N D and Tammela, T L J and Ulys, A and Vjaters, E and Polyakov, S and Jievaltas, M and Luz, M and Alekseev, B and Kuss, I and Le Berre, M.-A. and Snapir, A and Sarapohja, T and Fizazi, K | Efficacy and safety of darolutamide (DARO) in patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and a prostate-specific antigen doubling time (PSADT) > and ≤ 6 months.                                                | Oncology Research and Treatment                                                                                                                       | 2020 | 43      |        | 223-223     | Tipo de publicación equivocada |
| Bogemann, M W H and Shore, N D and Tammela, T L J and Ulys, A and Vjaters, E and Polyakov, S and Jievaltas, M and Luz, M and Alekseev, B and Kuss, I and al., et                                                                | Efficacy and safety of darolutamide (DARO) in patients with non-metastatic castration-resistant prostate cancer (nmCRPC) and a prostate-specific antigen doubling time (PSADT) >6 months                                                        | European urology open science                                                                                                                         | 2020 | 19      |        | e1389-e1390 | Tipo de publicación equivocada |
| Small, E J and Saad, F and Hadaschik, B A and Graff, J N and Mainwaring, P N and McQuarrie, K and Li, S and Lawson, J and Lopez-Gitlitz, A and Smith, M R                                                                       | Patient reported outcomes (PROS) in spartan, a phase 3, double-blind, randomized study of apalutamide (APA) plus androgen deprivation therapy (ADT) vs placebo plus ADT in men with nonmetastatic castration-resistant prostate cancer (NMCRPC) | Journal of urology                                                                                                                                    | 2018 | 199     | 4      | e703-e704   | Tipo de publicación equivocada |
| Azad, A and Ye, D-W and Uemura, H and Bhaumik, A and Eisbacher, M and Singh, A and McCarthy, S and Mundle, S D and Chi, K N and Agarwal, N                                                                                      | Efficacy and safety of apalutamide in metastatic castration sensitive prostate cancer patients with a prior history of cardiovascular or metabolic risk factors: a post-hoc analysis of the TITAN study                                         | Journal of clinical oncology                                                                                                                          | 2025 | 43      |        |             | Tipo de publicación equivocada |

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| Karsh, L I and Penson, D F and Concepcion, R and Flanders, S and Brown, B A and Yang, H and Ramaswamy, K and Schultz, N M                                                                                                                                                                 | Comparison of enzalutamide and bicalutamide in patients with non-metastatic castration-resistant prostate cancer: number needed to treat to achieve one additional patient free of clinical progression events      | Journal of clinical oncology | 2018 | 36      | 6      |         | Tipo de publicación equivocada |
| De Bono, J S and Fizazi, K and Saad, F and Taplin, M-E and Sternberg, C N and Miller, K and Mulders, P and Chi, K N and Armstrong, A J and Hirmand, M and al., et                                                                                                                         | Primary, secondary, and quality-of-life endpoint results from the phase III AFFIRM study of MDV3100, an androgen receptor signaling inhibitor                                                                       | Journal of clinical oncology | 2012 | 30      | 15     |         | Tipo de publicación equivocada |
| Devos, G and Tosco, L and Baldewijns, M and Gevaert, T and Goffin, K and Petit, V and Mai, C and Laenen, A and Raskin, Y and Van Haute, C and Goeman, L and De Meerleer, G and Berghen, C and Devlies, W and Claessens, F and Van Poppel, H and Everaerts, W and Joniau, S                | ARNEO: A Randomized Phase II Trial of Neoadjuvant Degarelix with or Without Apalutamide Prior to Radical Prostatectomy for High-risk Prostate Cancer                                                                | European Urology             | 2023 | 83      | 6      | 508-518 | Tratamiento equivocado         |
| G, Werutsky and FC, Maluf and EH, Cronemberger and V, Carrera Souza and SP, Dos Santos Martins and F, Peixoto and O, Smaletz and F, Schutz and D, Herchenhorn and T, Santos and F, Mavignier Carcano and D, Queiroz Muniz and PRS, Nunes Filho and F, Zaffaroni and C, Barrios and A, Fay | The LACOG-0415 phase II trial: abiraterone acetate and ADT versus apalutamide versus abiraterone acetate and apalutamide in patients with advanced prostate cancer with non-castration testosterone levels.         | BMC cancer                   | 2019 | 19      | 1      | 487-487 | Tipo de publicación equivocada |
| M, Mason and P, Richaud and Z, Bosnyak and A, Malmberg and A, Neijber                                                                                                                                                                                                                     | Degarelix Versus Goserelin Plus Bicalutamide in the Short-Term Relief of Lower Urinary Tract Symptoms in Prostate Cancer Patients: Results of a Pooled Analysis.                                                    | Lower urinary tract symptoms | 2017 | 9       | 2      | 82-88   | Artículo general               |
| Agarwal, N and Chowdhury, S and Bjartell, A and Chung, B H and De Santana Gomes, A J P and Given, R and Juarez, A and Merseburger, A S and                                                                                                                                                | Health-related quality of life (HRQoL) and patient-reported outcomes at final analysis of the TITAN study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate | Journal of clinical oncology | 2021 | 39      | 15     |         | Tipo de publicación equivocada |

| Autor                                                                                                                                                                           | Título                                                                                                                                                                                                                                | Revista                                                                                                                                                     | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Ozguroglu, M and Uemura, H and al., et                                                                                                                                          | cancer (mCSPC) receiving androgen deprivation                                                                                                                                                                                         |                                                                                                                                                             |      |         |        |           |                                |
|                                                                                                                                                                                 | ODENZA, a Prospective, Randomized, Open-Label, Multicenter, Cross-Over Phase 2 Trial of Preference Between Darolutamide and Enzalutamide in Men With Asymptomatic or Mildly Symptomatic Metastatic Castrate-Resistant Prostate Cancer | Clinical advances in hematology & oncology                                                                                                                  | 2021 | 19      | 8      | 16-17     | Tipo de publicación equivocada |
| K, Axcróna and S, Aaltomaa and da Silva CM and H, Ozen and JE, Damber and LB, Tankó and E, Colli and P, Klarskov                                                                | Androgen deprivation therapy for volume reduction, lower urinary tract symptom relief and quality of life improvement in patients with prostate cancer: degarelix vs goserelin plus bicalutamide.                                     | BJU international                                                                                                                                           | 2012 | 110     | 11     | 1721-1728 | No se encuentra texto completo |
| Chen, R C and Mazza, G L and Fruth, B and Xiao, H and Picus, J and Taplin, M E and Dorff, T B and Appleman, L J and Weckstein, D J and Patnaik, A and al., et                   | Health-related quality of life (HRQOL) results from PRESTO (AFT-19), a phase 3 randomized trial of intensification of androgen blockade in patients with high-risk biochemically relapsed castration sensitive prostate cancer        | Journal of clinical oncology                                                                                                                                | 2024 | 42      | 16     |           | Tipo de publicación equivocada |
| Siemens, D R and Klotz, L and Heidenreich, A and Chowdhury, S and Villers, A and Baron, B and Van Os, S and Hasabou, N and Brown, S and Wang, F and al., et                     | Efficacy and safety of enzalutamide versus bicalutamide in younger and older patients with metastatic castration-resistant prostate cancer in the terrain trial                                                                       | Asia-Pacific journal of clinical oncology                                                                                                                   | 2016 | 12      |        | 117-117   | Tipo de publicación equivocada |
| Fallara, G and Robesti, D and Nocera, L and Raggi, D and Marandino, L and Belladelli, F and Montorsi, F and Malavaud, B and Ploussard, G and Necchi, A and Martini, A           | Chemotherapy and advanced androgen blockage, alone or combined, for metastatic hormone-sensitive prostate cancer a systematic review and meta-analysis                                                                                | Cancer Treatment Reviews                                                                                                                                    | 2022 | 110     |        |           | Tratamiento equivocado         |
| EUCTR2010-021868-15-BE                                                                                                                                                          | A Randomized, Double-Blind, Phase II, Efficacy and Safety Study of MDV3100 (ASP9785) vs. Bicalutamide in Castrate Men with Metastatic Prostate Cancer                                                                                 | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2010-021868-15-BE">https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2010-021868-15-BE</a> | 2011 |         |        |           | Tipo de publicación equivocada |
| Rathkopf, D E and Smith, M R and De Bono, J S and Logothetis, C and Shore, N and De Souza, P L and Fizazi, K and Mulders, P and Mainwaring, P N and Hainsworth, J D and al., et | Long-term safety and efficacy analysis of abiraterone acetate (AA) plus prednisone (P) in metastatic castration-resistant prostate cancer (mCRPC) without prior chemotherapy (COU-AA-302)                                             | Journal of clinical oncology                                                                                                                                | 2013 | 31      | 15     |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Título                                                                                                                                                                                                                                                    | Revista                                                                                                                                                                             | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| De Giorgi, U F F and Freedland, S J and Gleave, M E and Tutrone, R and Bailen, J L and Roos, E and Kliment, J and Marx, G M and Karsh, L I and Ramirez-Backhaus, M and al., et                                                                                                                                                                                                                                                                                          | 1777P Enzalutamide (enza) monotherapy for the treatment (tx) of prostate cancer with high-risk biochemical recurrence (BCR): EMBARK secondary endpoints                                                                                                   | Annals of oncology                                                                                                                                                                  | 2023 | 34      |        | S960-S961 | Tipo de publicación equivocada |
| ISRCTN64733264                                                                                                                                                                                                                                                                                                                                                                                                                                                          | A phase III study of neoadjuvant bicalutamide in patients with intermediate risk prostate cancer undergoing radiation therapy                                                                                                                             | <a href="https://trialsearch.worldwideclinicaltrials.com/Trial2.aspx?TrialID=ISRCTN64733264">https://trialsearch.worldwideclinicaltrials.com/Trial2.aspx?TrialID=ISRCTN64733264</a> | 2005 |         |        |           | Tipo de publicación equivocada |
| P, Schellhammer and R, Sharifi and N, Block and M, Soloway and P, Venner and AL, Patterson and M, Sarosdy and N, Vogelzang and J, Jones and G, Kolvenbag                                                                                                                                                                                                                                                                                                                | Maximal androgen blockade for patients with metastatic prostate cancer: outcome of a controlled trial of bicalutamide versus flutamide, each in combination with luteinizing hormone-releasing hormone analogue therapy. Casodex Combination Study Group. | Urology                                                                                                                                                                             | 1996 | 47      | 1      | 54-54     | Tipo de publicación equivocada |
| G, Gravis and K, Fizazi and F, Joly and S, Oudard and F, Priou and B, Esterni and I, Latorzeff and R, Delva and I, Krakowski and B, Laguerre and F, Rolland and C, Théodore and G, Deplanque and JM, Ferrero and D, Pouessel and L, Mourey and P, Beuzeboc and S, Zanetta and M, Habibian and JF, Berdah and J, Dauba and M, Baciuchka and C, Platini and C, Linassier and JL, Labourey and JP, Machiels and C, El Kouri and A, Ravaud and E, Suc and JC, Eymard and A, | Androgen-deprivation therapy alone or with docetaxel in non-castrate metastatic prostate cancer (GETUG-AFU 15): a randomised, open-label, phase 3 trial.                                                                                                  | The Lancet. Oncology                                                                                                                                                                | 2013 | 14      | 2      | 149-158   | Comparación equivocada         |

| Autor                                                                                                                                                                                             | Título                                                                                                                                                                                                                                                                                                        | Revista                                                                                                                                               | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Hasbini and G, Bousquet and M, Soulie                                                                                                                                                             |                                                                                                                                                                                                                                                                                                               |                                                                                                                                                       |      |         |        |           |                                |
| P, Hoskin and O, Sartor and JM, O'Sullivan and DC, Johannessen and SI, Helle and J, Logue and D, Bottomley and S, Nilsson and NJ, Vogelzang and F, Fang and M, Wahba and AK, Aksnes and C, Parker | Efficacy and safety of radium-223 dichloride in patients with castration-resistant prostate cancer and symptomatic bone metastases, with or without previous docetaxel use: a prespecified subgroup analysis from the randomised, double-blind, phase 3 ALSYMPCA trial.                                       | The Lancet. Oncology                                                                                                                                  | 2014 | 15      | 12     | 1397-1406 | No se encuentra texto completo |
| CTRI/2021/03/032172                                                                                                                                                                               | Phase 3 study of oral drug, darolutamide in addition to androgen deprivation therapy (ADT) versus placebo plus ADT in men with metastatic hormone-sensitive prostate cancer (mHSPC), that has spread to other parts of body (metastatic)                                                                      | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2021/03/032172">https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2021/03/032172</a> | 2021 |         |        |           | Tipo de publicación equivocada |
| Sartor, O and Lenzo, N and Cade, D and Agarwal, N                                                                                                                                                 | A PHASE 3 STUDY OF 177LU-TLX591 PLUS SOC VS SOC ALONE IN PATIENTS WITH MCRPC (PROSTACT GLOBAL)                                                                                                                                                                                                                | Urologic oncology: seminars and original investigations                                                                                               | 2025 | 43      | 3      | 2-2       | Tipo de publicación equivocada |
| JE, Frampton and KA, Lyseng-Williamson                                                                                                                                                            | Degarelix.                                                                                                                                                                                                                                                                                                    | Drugs                                                                                                                                                 | 2009 | 69      | 14     | 1967-1976 | Tipo de publicación equivocada |
| E, Scott                                                                                                                                                                                          | Androgen deprivation with or without radiation therapy for clinically node-positive prostate cancer. Lin CC, Gray PJ, Jemal A, Efsthathiou JA, Surveillance and Health Services Research Program, Intramural Research, American Cancer Society, Atlanta, GA (CCL, AJ); Department of Radiation Oncology, M... | Urologic oncology                                                                                                                                     | 2017 | 35      | 3      | 122-123   | Tipo de publicación equivocada |
| F, Montorsi and G, Gandaglia and F, Barletta and A, Briganti                                                                                                                                      | Re: Bertrand F. Tombal, Francisco Gomez-Veiga, Alvaro Gomez-Ferrer, et al. A Phase 2 Randomized Open-label Study of Oral Darolutamide Monotherapy Versus Androgen Deprivation Therapy in Men with Hormone-sensitive Prostate Cancer (EORTC-GUCG 1532). Eur Urol Oncol 2024;7:1051-60.                         | European urology oncology                                                                                                                             | 2025 | 8       | 3      | 856-856   | Tipo de publicación equivocada |
| F, Sun and O, Oyesanmi and J, Fontanarosa and J, Reston and T, Guzzo and K, Schoelles                                                                                                             | No Title                                                                                                                                                                                                                                                                                                      |                                                                                                                                                       | 2014 |         |        |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                 | Título                                                                                                                                                                              | Revista                                         | Año  | Volumen | Número | Páginas       | Razón de exclusión             |
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| P, Dahm and M, Brasure and E, Ester and EJ, Linskens and R, MacDonald and VA, Nelson and C, Ryan and J, Saha and S, Sultan and KE, Ullman and TJ, Wilt                                | No Title                                                                                                                                                                            |                                                 | 2020 |         |        |               | Tipo de publicación equivocada |
| Moussa, Mohamad and Papatsoris, Athanasios and Dellis, Athanasios and Chakra, Mohamed Abou and Fragkoulis, Charalampos                                                                | Current and emerging gonadotropin-releasing hormone (GnRH) antagonists for the treatment of prostate cancer                                                                         | Expert opinion on pharmacotherapy               | 2021 | 22      | 17     | 2373-2381     | No se encuentra texto completo |
| Zhao, Jing and Chen, Junru and Sun, Guangxi and Shen, Pengfei and Zeng, Hao                                                                                                           | Luteinizing hormone-releasing hormone receptor agonists and antagonists in prostate cancer: effects on long-term survival and combined therapy with next-generation hormonal agents | Cancer Biology & Medicine                       | 2024 | 21      | 11     | 1012-1032     | Tipo de publicación equivocada |
| Modi, Dimple and Hussain, Md Sadique and Ainampudi, Swetha and Prajapati, Bhupendra G                                                                                                 | Long acting injectables for the treatment of prostate cancer                                                                                                                        | Journal of Drug Delivery Science and Technology | 2024 |         |        | 105996-105996 | Tipo de publicación equivocada |
| Osborne, C K and Blumenstein, B and Crawford, E D and Coltman, C A and Smith, A Y and Lambuth, B W and Chapman, R A                                                                   | Combined versus sequential chemo-endocrine therapy in advanced prostate cancer: final results of a randomized Southwest Oncology Group study                                        | Journal of clinical oncology                    | 1990 | 8       | 10     | 1675-1682     | Tratamiento equivocado         |
| Van Poppel, Hendrik and De La Rosette, J J and Persson, B E and Olesen, T K                                                                                                           | 23 Long-Term Evaluation of Degarelix, a Gonadotrophin-Releasing Hormone (GNRH) Receptor Blocker, Investigated in a Multicentre Randomised Study in Prostate Cancer (CAP) Patients   | European Urology Supplements                    | 2007 | 6       | 2      | 28-28         | Tipo de publicación equivocada |
| Fallara, G and Belladelli, F and Robesti, D and Raggi, D and Nocera, L and Marandino, L and Galsky, M D and Montorsi, F and Malavaud, B and Ploussard, G and Necchi, A and Martini, A | Androgen annihilation versus advanced androgen blockage as first line treatment for metastatic castration resistant prostate cancer: A systematic review and meta-analysis          | Critical Reviews in Oncology/Hematology         | 2022 | 179     |        |               | Tratamiento equivocado         |
| Maughan, B L and Kessel, A and McFarland, T R and Sayegh, N and Nussenzeig, R and Hahn, A W and Hoffman,                                                                              | Radium-223 plus Enzalutamide Versus Enzalutamide in Metastatic Castration-Refractory Prostate Cancer: final Safety and Efficacy Results                                             | Oncologist                                      | 2021 | 26      | 12     | 1006-e2129    | Tratamiento equivocado         |



| Autor                                                                                                                                                                                                                                                                                                                 | Título                                                                                                                                                                                                              | Revista                               | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| J M and Morton, K and Sirohi, D and Kohli, M and al., et                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                     |                                       |      |         |        |           |                                |
| de Incorporação de Tecnologias no Sistema Único de Saúde (Conitec), Brasil. Comissão Nacional                                                                                                                                                                                                                         | Abiraterona, apalutamida, darolutamida e enzalutamida para o tratamento de indivíduos com câncer de próstata sensível à castração e metastático (CPSCm)                                                             |                                       | 2024 |         |        |           | Diseño de estudio equivocado   |
| Chi, K and Protheroe, A and Rodriguez Antolin, A and Facchini, G and Suttman, H and Matsubara, N and Ye, Z-Q and Keam, B and Li, T and McQuarrie, K and al., et                                                                                                                                                       | Benefits of abiraterone acetate plus prednisone (AA1P) when added to androgen deprivation therapy (ADT) in LATITUDE on patient (Pt) reported outcomes (PRO)                                                         | Annals of oncology                    | 2017 | 28      |        | v269-v269 | Tipo de publicación equivocada |
| del Seguro Social (ISSS), El Salvador. Instituto Salvadoreño                                                                                                                                                                                                                                                          | Revisión de grupos farmacológicos en el tratamiento de cáncer de próstata                                                                                                                                           |                                       | 2024 |         |        |           | Tipo de publicación equivocada |
| James, N D and De Bono, J S and Spears, M R and Clarke, N and Mason, M D and Dearnaley, D and Ritchie, A W S and Russell, J M and Gilson, C and Jones, R J and Gillesen, S and Matheson, D and Aung, S and Birtle, A J and Chowdhury, S and Gale, J and Malik, Z and O'Sullivan, J M and Parmar, M K B and Sydes, M R | Adding abiraterone for men with high-risk prostate cancer (PCa) starting longterm androgen deprivation therapy (ADT): Survival results from STAMPEDE (NCT00268476)                                                  | Journal of Clinical Oncology          | 2017 | 35      | 15     |           | Tipo de publicación equivocada |
| Chi, K N and Annala, M and Sunderland, K and Khalaf, D and Finch, D and Oja, C D and Vergidis, J and Zulfiqar, M and Beja, K and Vandekerkhove, G and al., et                                                                                                                                                         | A randomized phase II cross-over study of abiraterone + prednisone (ABI) vs enzalutamide (ENZ) for patients (pts) with metastatic, castration-resistant prostate cancer (mCRPC)                                     | Journal of clinical oncology          | 2017 | 35      | 15     |           | Tipo de publicación equivocada |
| del Seguro Social (ISSS), El Salvador. Instituto Salvadoreño                                                                                                                                                                                                                                                          | Enzalutamida en 3° y 4° línea de tratamiento en cáncer de próstata hormono resistente, metastásico                                                                                                                  |                                       | 2024 |         |        |           | Tipo de publicación equivocada |
| H, Akaza and A, Yamaguchi and T, Matsuda and M, Igawa and H, Kumon and A, Soeda and Y, Arai and M, Usami and S, Naito and H, Kanetake and Y, Ohashi                                                                                                                                                                   | Superior anti-tumor efficacy of bicalutamide 80 mg in combination with a luteinizing hormone-releasing hormone (LHRH) agonist versus LHRH agonist monotherapy as first-line treatment for advanced prostate cancer: | Japanese journal of clinical oncology | 2004 | 34      | 1      | 20-28     | No se encuentra texto completo |

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|                                                                                                                                                                                | interim results of a randomized study in Japanese patients.                                                                                                                                                                                                                                               |                                                                                                                                                                           |      |         |        |         |                                |
| de Evaluación de Tecnologías Sanitarias (RENETSA), Perú. Red Nacional and de Evaluación de Tecnologías en Salud e Investigación (IETSI). Seguro Social de S..., Perú. Insti... | Darolutamida para el tratamiento de hombres adultos con cáncer de próstata resistente a la castración no metastásico con alto riesgo de desarrollar enfermedad metastásica                                                                                                                                |                                                                                                                                                                           | 2023 |         |        |         | No se encuentra texto completo |
| IRCT20120618010057N2                                                                                                                                                           | The effect of addition of low dose abiraterone to the ADT+RT in local recurrent prostate cancers                                                                                                                                                                                                          | <a href="https://trialsearch.worldwideint.org/Trial2.aspx?TrialID=IRCT20120618010057N2">https://trialsearch.worldwideint.org/Trial2.aspx?TrialID=IRCT20120618010057N2</a> | 2022 |         |        |         | Tipo de publicación equivocada |
| de Evaluación de Tecnologías en Salud e Investigación-IETSI (Peru), Instituto                                                                                                  | Eficacia y seguridad de enzalutamida en pacientes adultos con cáncer de próstata resistente a la castración metastásico, con progresión a quimioterapia basada en docetaxel, y tienen contraindicaciones al uso, o desarrollan reacciones adversas que lleven a la interrupción de acetato de abiraterona |                                                                                                                                                                           | 2023 |         |        |         | No se encuentra texto completo |
| Lukka, H and Pugh, S L and Shipley, W U and Major, P and Sartor, A O and Dayes, I S and Bahary, J-P and Efsthathiou, J A and Pisansky, T M and Zeitzer, K L and al., et        | Long-term results of radiation with or without anti-androgens (AAT) in patients receiving salvage prostate bed radiation therapy (sRT) post prostatectomy                                                                                                                                                 | Journal of clinical oncology                                                                                                                                              | 2024 | 42      | 4      |         | Tipo de publicación equivocada |
| Carles, J and Davis, I and De Bono, J S and Fizazi, K and Gerritsen, W and Rathkopf, D E and Ryan, C J and Saad, F and Steuber, T and Wilding, G and al., et                   | Safety of long-term (LT) treatment (tmt) of chemotherapy (chemo)-naïve metastatic castration-resistant prostate cancer (mCRPC) patients (pts) with abiraterone acetate plus prednisone (AA + P) for ≥ 4 years (yrs)                                                                                       | Annals of oncology                                                                                                                                                        | 2016 | 27      |        |         | Tipo de publicación equivocada |
| Sun, Y and Ye, D and Huang, Y and Zhou, F and Xie, K and Matveev, V and Li, C and Alexeev, B and Tian, Y and Qiu, M and al., et                                                | Efficacy and safety of abiraterone acetate in asymptomatic or mildly symptomatic chemotherapy-naïve patients with metastatic castrationresistant prostate cancer: a phase III, double-blind, randomized, placebo-controlled study conducted in China, Malaysia,                                           | BJU international                                                                                                                                                         | 2015 | 116     |        | 2-2     | Tipo de publicación equivocada |
| de Enfermedades Neoplásicas, Instituto Nacional                                                                                                                                | Eficacia y seguridad del uso de acetato de abiraterona en pacientes con cáncer de próstata metastásico resistente a la                                                                                                                                                                                    |                                                                                                                                                                           | 2022 |         |        |         | No se encuentra                |

| Autor                                                                                                                                                                     | Título                                                                                                                                                                                                                                                                                                       | Revista                                   | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
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|                                                                                                                                                                           | castración, en el escenario pre y post quimioterapia                                                                                                                                                                                                                                                         |                                           |      |         |        |                 | texto completo                 |
| Fizazi, K and Feyerabend, S and Matsubara, N and Ozguroglu, M and Fein, L E and Antolin, A R and Alekseev, B Y and Sulur, G and Protheroe, A and De Porre, P and al., et  | Longer term preplanned efficacy and safety analysis of abiraterone acetate + prednisone (AA + P) in patients (pts) with newly diagnosed high-risk metastatic castrationnaïve prostate cancer (NDx-HR mCNPC) from the phase 3 LATITUDE trial                                                                  | Journal of clinical oncology              | 2018 | 36      | 15     |                 | Tipo de publicación equivocada |
| Francolini, G and Detti, B and Di Cataldo, V and Caini, S and Bruni, A and Ingrosso, G and D'angelillo, R M and Alitto, A R and Augugliaro, M and Triggiani, L and et al. | Stereotactic body radiation therapy and abiraterone acetate for patients affected by oligometastatic castrate-resistant prostate cancer: freedom from biochemical, radiological progression free survival and freedom from following treatment approaches within a randomized phase II trial (ARTO – NCT0... |                                           | 2023 | 57      |        | S157-S158       | Tipo de publicación equivocada |
| Small, E J and Cella, D and McQuarrie, K and Saad, F and Hadaschik, B A and Graff, J N and Uemura, H and Oudard, S and Yu, M K and Hudgens, S and al., et                 | Health-related quality of life (HRQoL) after progressive disease (PD) in SPARTAN: a phase III trial of apalutamide (APA) versus placebo (PBO) in men with nonmetastatic castration-resistant prostate cancer (nmCRPC)                                                                                        | Annals of oncology                        | 2018 | 29      |        | viii276-viii277 | Tipo de publicación equivocada |
| Heidenreich, A and Chowdhury, S and Klotz, L and Siemens, D R and Villers, A and Ivanescu, C and Holmstrom, S and Baron, B and Wang, F and Forer, D and al., et           | Impact of enzalutamide (ENZA) compared with bicalutamide (BIC) on quality of life (QoL) in men with metastatic castration-resistant prostate cancer (mCRPC): results from the TERRAIN study                                                                                                                  | European journal of cancer                | 2015 | 51      |        | S495-S495       | Tipo de publicación equivocada |
| Sargos, P and Mottet, N and Richaud, P                                                                                                                                    | Long-term androgen deprivation, with or without radiotherapy, in locally-advanced prostate cancer: results from a phase iii randomized study                                                                                                                                                                 | Journal of urology                        | 2017 | 197     | 4      | e1361-e1361     | No se encuentra texto completo |
| da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos                                                                                                        | Abiraterona para câncer de próstata metastático resistente à castração em pacientes com uso prévio de quimioterapia                                                                                                                                                                                          |                                           | 2019 |         |        |                 | Tipo de publicación equivocada |
| Oliveira, N and Shore, N and Fizazi, K and Tammela, T and Luz, M and Salas, M P and Quellet, P and Lago, S and                                                            | Analysis of the Effect of Crossover From Placebo (PBO) to Darolutamide (DARO) on Overall Survival (OS) Benefit in the ARAMIS Trial                                                                                                                                                                           | Asia-Pacific journal of clinical oncology | 2021 | 17      |        | 39-40           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                            | Título                                                                                                                                                                                                                                  | Revista                      | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Bastos, D and Jansz, G K and al., et                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                         |                              |      |         |        |           |                                |
| Fizazi, K and Tran, N and Fein, L E and Matsubara, N and Bjartell, A and Galli, L and Lee, J-L and Mazhar, D and North, S A and Olmos, D and al., et                                                                                                                             | Abiraterone acetate (AA) plus prednisone (P) 5 mg QD in metastatic castration-naïve prostate cancer (mCNP): detailed safety analyses from the LATITUDE phase 3 trial                                                                    | Journal of clinical oncology | 2018 | 36      | 6      |           | Tipo de publicación equivocada |
| Izumi, K and Mizokami, A                                                                                                                                                                                                                                                         | Dose modification in enzalutamide and abiraterone plus prednisolone for castration-resistant prostate cancer: Sub-analysis from ENABLE for PCa, a multicenter, randomized controlled trial                                              | Journal of Clinical Oncology | 2024 | 42      | 4      |           | Tipo de publicación equivocada |
| de Evaluación Tecnológica en Salud, Instituto                                                                                                                                                                                                                                    | Efectividad y seguridad de la bicalutamida como terapia hormonal adyuvante en pacientes con cáncer de próstata local y localmente avanzado                                                                                              |                              | 2013 |         |        | 4-4       | Tipo de publicación equivocada |
| Shore, N and Rathkopf, D and Smith, M R and De Bono, J S and Logothetis, C and De Souza, P and Fizazi, K and Mulders, P F A and Mainwaring, P and Hainsworth, J D and al., et                                                                                                    | Efficacy and long-term safety analysis of study COU-AA-302: abiraterone acetate plus prednisone in chemotherapy-naïve metastatic castration-resistant prostate cancer                                                                   | Journal of urology           | 2014 | 191     | 4      | e764-e764 | Tipo de publicación equivocada |
| Okamura, T and Izumi, K and Kurokawa, S and Shima, T and Kato, Y and Mita, K and Kamiyama, M and Inoue, S and Hoshi, S and Tanaka, N and Yoshio, Y and Enokida, H and Chikazawa, I and Kawai, N and Hashimoto, K and Fukagai, T and Shigehara, K and Takahara, S and Mizokami, A | Efficacy and Safety of Enzalutamide and Abiraterone Plus Prednisolone in Elder Castration-Resistant Prostate Cancer Patients: A Sub-Analysis From the ENABLE Study                                                                      | Prostate                     | 2025 | 85      | 10     | 903-911   | Comparación equivocada         |
| Abdel-Aty, H and Amos, C L and Brown, L C and Yogeswaran, Y and Niem, P and Dutey-Magni, P and Kasivisvanathan, V and Bennett, R and Clarke, N and Sachdeva, A and al., et                                                                                                       | 1657TiP The STAMPEDE2 stereotactic ablative body radiotherapy (SABR) trial: a phase III, randomised, open-label trial in patients with newly diagnosed oligometastatic prostate cancer (PC) starting androgen deprivation therapy (ADT) | Annals of oncology           | 2024 | 35      |        | S999-S999 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                                | Título                                                                                                                                                                    | Revista                                                 | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Shore, N and Morgans, A K and Boegemann, M and Gallagher, E and Paracha, N and Serafini, P and Pushkarna, D and Pourrahmat, M.-M. and Kurt, M and Abrams, K R                                                                                                                                                        | Radiological progression-free survival as a surrogate for overall survival in patients with metastatic hormone-sensitive prostate cancer: A bivariate meta-analysis       | European Journal of Cancer                              | 2025 | 223     |        |           | Desenlace equivocado           |
| Lu, J and Zhang, F and Liu, M and Tengting, J                                                                                                                                                                                                                                                                        | An Updated Systematic Review and Network Meta-Analysis on Combination Therapies for Metastatic Hormone-Sensitive Prostate Cancer with High- Versus Low-Volume Diseases    | SSRN                                                    | 2025 |         |        |           | Comparación equivocada         |
| Yaxley, J W and Fitzgerald, B                                                                                                                                                                                                                                                                                        | Cardiovascular risks of androgen receptor targeted agents in prostate cancer: a systematic review and meta-analysis "PCAN-23-0763R"                                       | Prostate Cancer and Prostatic Diseases                  | 2025 | 28      | 2      | 247-248   | Tipo de publicación equivocada |
| Odat, R M and Jain, H and Jain, J and Alshwayyat, S and Alshwayyat, M and Yasin, J A and Zyoud, A and Alkadomi, O and Rababah, M K and Alfreijat, T M and Ahmad, N S and Nguyen, D and Gole, S                                                                                                                       | Risk of cardiovascular disease following degarelix versus gonadotropin-releasing hormone agonists in patients with prostate cancer: a systematic review and meta-analysis | Urologic Oncology: Seminars and Original Investigations | 2025 | 43      | 6      | 359-369   | Desenlace equivocado           |
| Francini, E and Agarwal, N and Castro, E and Cheng, H H and Chi, K N and Clarke, N and Mateo, J and Rathkopf, D and Saad, F and Tombal, B                                                                                                                                                                            | Intensification Approaches and Treatment Sequencing in Metastatic Castration-resistant Prostate Cancer: A Systematic Review                                               | European Urology                                        | 2025 | 87      | 1      | 29-46     | Tratamiento equivocado         |
| Naqvi, S A A and Riaz, I B and Bibi, A and Khan, M A and Imran, M and Khakwani, K Z R and Raina, A and Anjum, M U and Cobran, E K and Warner, J L and Hussain, S A and Singh, P and Childs, D S and Baca, S C and Orme, J J and Mateo, J and Agarwal, N and Gillissen, S and Murad, M H and Sartor, O and Bryce, A H | Heterogeneity of the Treatment Effect with PARP Inhibitors in Metastatic Castration-resistant Prostate Cancer: A Living Interactive Systematic Review and Meta-analysis   | European Urology                                        | 2025 | 87      | 6      | 626-640   | Comparación equivocada         |
| Small, E J and Lee, J Y and Lopez-Gitlitz, A and Saad, F and Rooney, B and Hadaschik,                                                                                                                                                                                                                                | Prostate-specific antigen (PSA) outcomes in patients (pts) with nonmetastatic castration-resistant prostate cancer (NMCRPC) treated                                       | Journal of urology                                      | 2018 | 199     | 4      | e232-e232 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                     | Título                                                                                                                                                                                                                                                        | Revista                           | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
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| B A and Uemura, H and Shu, Y and Yu, M and Smith, M R                                                                                                                     | with apalutamide (APA): results from phase 3 spartan study                                                                                                                                                                                                    |                                   |      |         |        |                 |                                |
| Belabaci, Z and Mose, L and El-Taji, O and Otmani, Z and Hannouneh, Z A and Mohamad, I and Zilli, T and Mohamad, O and Pervez, N and Arafat, W and Vogl, U and Shelan, M  | Safety and Efficacy of Reduced Dose of Enzalutamide in Patients with Castration-Resistant Prostate Cancer: A Systematic Review                                                                                                                                | Pharmaceuticals                   | 2025 | 18      | 5      |                 | Comparación equivocada         |
| Chowdhury, S and Bjartell, A and Merseburger, A and Chung, B and Uemura, H and Ye, D and Ozguroglu, M and De Santana Gomes, A and Juarez Soto, A and Given, R and al., et | Apalutamide (apa) for metastatic castration-sensitive prostate cancer (mcspsc): outcomes in high-volume (hv) and low-volume (lv) disease from the titan final analysis (fa)                                                                                   | European urology                  | 2021 | 79      |        | S1180-S1181     | Tipo de publicación equivocada |
| Omar Fahmy, O F and Mohd Razaleigh Yusof, M R Y and Mohd Ghani Khairul Asri, M.G.K.A.                                                                                     | Efficacy and Side Effects of Lutetium-177 PSMA-617 in Patients with Castration Resistant Metastatic Prostate Cancer: A Systematic Review and Meta- analysis                                                                                                   | Urologiia (Moscow, Russia : 1999) | 2025 |         | 2      | 105-113         | No se encuentra texto completo |
| Fizazi, K and Morris, M J and Shore, N D and Chi, K N and Crosby, M and De Bono, J S and Herrmann, K and Roubaud, G and Nagarajah, J and Fleming, M T and al., et         | Health-related quality of life and pain in a phase 3 study of [177Lu]Lu-PSMA-617 in taxane-naïve patients with metastatic castration-resistant prostate cancer (PSMAfore)                                                                                     | Journal of clinical oncology      | 2024 | 42      | 16     |                 | Tipo de publicación equivocada |
| Patel, S and Zhu, K and CV, Dave and Ghajar, M and Zhang, Y and Saraiya, B and EV, Bandera and Khosrow-Khavar, F                                                          | Comparative Cardiovascular Safety of Gonadotropin-releasing Hormone Antagonists and Agonists Among Patients Diagnosed with Prostate Cancer: A Systematic Review and Meta-analysis of Real-world Evidence Studies. PG - 510-519 LID - S2588-9311(24)00213-X [p |                                   |      |         | 2588   |                 | Tipo de publicación equivocada |
| Herrmann, K and Sartor, O and Castellano, D and De Bono, J and Shore, N and Chi, K and Crosby, M and Piulats, J and Flechon, A and Wei, X and al., et                     | Phase 3 trial of [177Lu]Lu-PSMA-617 in taxanenaïve patients with metastatic castration resistant prostate cancer (PSMAfore)                                                                                                                                   | Journal of nuclear medicine       | 2024 | 65      |        |                 | Tipo de publicación equivocada |
| Gao, X and Smith, M R and Scher, H I and Verholen, F and Adorjan, P and                                                                                                   | A phase 2, randomized, open-label study comparing the effects of darolutamide versus enzalutamide monotherapy on serum                                                                                                                                        | Journal of clinical oncology      | 2023 | 41      | 16     | TPS5111-TPS5111 | Tipo de publicación equivocada |

| Autor                                                                                                                                                             | Título                                                                                                                                                                                                                                                           | Revista                      | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Dissanayake, M and Laccetti, A L                                                                                                                                  | testosterone levels in patients with hormone-naive prostate cancer: ARAMON study                                                                                                                                                                                 |                              |      |         |        |           |                                |
| Witjes, W P and Schulman, C C and Debruyne, F M                                                                                                                   | Preliminary results of a prospective randomized study comparing radical prostatectomy versus radical prostatectomy associated with neoadjuvant hormonal combination therapy in T2-3 N0 M0 prostatic carcinoma. The European Study Group on Neoadjuvant Treatment | Urology                      | 1997 | 49      | 3      | 65-69     | Tratamiento equivocado         |
| Shore, N D and Sieber, P R and Gleave, M and De Giorgi, U and Mehlhaff, B A and Danila, D C and Dunshee, C and Lallas, C D and Pliskin, M and Tang, Y and al., et | Outcomes of men with high-risk biochemically recurrent prostate cancer who suspended enzalutamide monotherapy treatment in the phase 3 EMBARK study                                                                                                              | Journal of clinical oncology | 2024 | 42      | 4      |           | Tipo de publicación equivocada |
| Carvalho, G F and Pires, I and Sudo, R Y U and Da Silva Gobbo, M O and Filho, N M                                                                                 | Association of androgen deprivation therapy and acute kidney injury in patients with prostate cancer: A systematic review and meta-analysis                                                                                                                      | Journal of Clinical Oncology | 2025 | 43      |        |           | Tipo de publicación equivocada |
| Shore, N D and Morgans, A K and Paracha, N and Thom, H and Keeney, E and Orishaba, P and Phillippo, D and Aceituno, D and Wallis, C J D and Boegemann, M          | Population-adjusted network meta-analyses (NMA) to evaluate the efficacy of treatment alternatives for metastatic hormone-sensitive prostate cancer (mHSPC)                                                                                                      | Journal of Clinical Oncology | 2025 | 43      |        |           | Tipo de publicación equivocada |
| Fizazi, K and Morris, M J and Shore, N D and Chi, K N and Crosby, M and de Bono, J S and Herrmann, K and Roubaud, G and Nagarajah, J and Fleming, M T and al., et | 1599P Symptomatic skeletal events, health-related quality of life and pain in a phase III study of [177Lu]Lu-PSMA-617 in taxane-naive patients with PSMA-positive metastatic castration-resistant prostate cancer: third interim analysis of PSMAfore            | Annals of oncology           | 2024 | 35      |        | S964-S965 | Tipo de publicación equivocada |
| Lunan, M and Raval, A D and Phan, N T N and Korn, M J and Quintero, V and McKay, R R                                                                              | Effectiveness and safety of life outcomes in men with metastatic castration-resistant prostate cancer (mCRPC): A systematic literature review of 48 real-world studies                                                                                           | Journal of Clinical Oncology | 2025 | 43      |        |           | Tipo de publicación equivocada |
| Izumi, K and Mizokami, A                                                                                                                                          | Long follow-up quality of life outcomes from an investigator-initiated randomized trial of enzalutamide versus abiraterone plus prednisolone in docetaxel-untreated castration-resistant prostate cancer                                                         | Journal of Clinical Oncology | 2025 | 43      |        |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                  | Título                                                                                                                                                                                                                         | Revista                                 | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Pieczonka, C and Smith, M and Fizazi, K and Tammela, T and Cruz, F M and Nordquist, L and Emmenegger, U and Silveira, G and Concepcion, R and Paula, A and al., et                                                     | Safety of darolutamide (DARO) for non-metastatic castration-resistant prostate cancer (nmCRPC) from extended followup in the phase 3 ARAMIS trial                                                                              | Canadian urological association journal | 2021 | 15      | 9      | S235-S235   | Tipo de publicación equivocada |
| Saad, F and Shore, N D and Vjaters, E and Olmos, D and Littleton, N and Liu, A and Testa, I and Mo, M and Srinivasan, S and Haresh, K P                                                                                | Darolutamide plus ADT in patients with metastatic hormone-sensitive prostate cancer (mHSPC) by disease volume: subgroup analysis of the phase 3 ARANOTE trial                                                                  | Journal of clinical oncology            | 2025 | 43      |        |             | Tipo de publicación equivocada |
| Petrylak, D P and Vogelzang, N J and Budnik, N and Wiechno, P J and Sternberg, C N and Doner, K and Bellmunt, J and Burke, J M and de Olza, M O and Choudhury, A and al., et                                           | Docetaxel and prednisone with or without lenalidomide in chemotherapy-naive patients with metastatic castration-resistant prostate cancer (MAINSAIL): a randomised, double-blind, placebo-controlled phase 3 trial             | The lancet. Oncology                    | 2015 | 16      | 4      | 417-425     | Tratamiento equivocado         |
| Francolini, G and Di Cataldo, V and Garlatti, P and Detti, B and Caini, S and Bruni, A and Ingrosso, G and D'Angelillo, R M and Alitto, A R and Augugliaro, M and al., et                                              | ARTO trial: overall survival analysis from a randomized phase II trial testing the benefit of adding stereotactic body radiotherapy to abiraterone acetate in patients with oligometastatic castrate-resistant prostate cancer | Journal of clinical oncology            | 2024 | 42      | 4      |             | Tipo de publicación equivocada |
| Miszczek, M and Fazekas, T and Rajwa, P and Matsukawa, A and Tsuboi, I and Leapman, M S and Kramer, G and Hussain, M and Merseburger, A and Briganti, A and D'Amico, A V and Gillessen, S and Saad, F and Shariat, S F | Prostate-specific Antigen Response as a Prognostic Factor for Overall Survival in Patients with Prostate Cancer Treated with Androgen Receptor Pathway Inhibitors: A Systematic Review and Meta-analysis                       | European Urology Focus                  | 2025 |         |        |             | Desenlace equivocado           |
| Ryan, C J and Smith, M R and Fizazi, K and Miller, K and Mulders, P and Sternberg, C N and Saad, F and Griffin, T and De Porre, P and Park, Y C and al., et                                                            | Final Overall Survival (Os) Analysis of Cou-Aa-302, a Randomized Phase 3 Study of Abiraterone Acetate (Aa) in Metastatic Castration-Resistant Prostate Cancer (Mcrpc) Patients (Pts) Without Prior Chemotherapy                | Annals of oncology                      | 2014 | 25      |        | iv255-iv255 | Tipo de publicación equivocada |
| Fazekas, T and Miszczyk, M and Giesen, A and Kóí, T and Zattoni, F and Rodriguez-Sanchez, L and Yanagisawa, T                                                                                                          | Androgen Receptor Pathway Inhibitor Monotherapy in Prostate Cancer: Safety, Oncologic Outcomes, and Quality of Life—A Systematic Review and Meta-analysis                                                                      | European Urology Focus                  | 2025 |         |        |             | Comparación equivocada         |



| Autor                                                                                                                                                                                                                                                                                        | Título                                                                                                                                                                                                                                                        | Revista                                                    | Año  | Volumen | Número | Páginas    | Razón de exclusión             |
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| and Matsukawa, A and Szarvas, T and Kryst, P and Rivas, J G and Merseburger, A S and Santis, M D and Joniau, S and Briganti, A and Marra, G and Nyirady, P and Gandaglia, G and Shariat, S F and Rajwa, P                                                                                    |                                                                                                                                                                                                                                                               |                                                            |      |         |        |            |                                |
| Mulders, P F A and Smith, M R and Fizazi, K and Saad, F and Sternberg, C N and Miller, K and Logothetis, C J and Shore, N D and Small, E J and Carles, J and al., et                                                                                                                         | Abiraterone acetate improves overall survival in chemotherapy-naïve metastatic castrationresistant prostate cancer (mCRPC): impact of crossover and baseline prognostic factors in the COU-AA-302 final analysis                                              | European urology, supplements                              | 2015 | 14      | 2      | e556-e556a | Tipo de publicación equivocada |
|                                                                                                                                                                                                                                                                                              | A Multicenter, Randomized Controlled Trial of Abiraterone Acetate (II) Combined with ADT Versus Abiraterone Acetate Combined with ADT in Patients with Metastatic Castration-resistant Prostate Cancer                                                        | <a href="http://clinicaltrials.gov">clinicaltrials.gov</a> | 2024 |         |        |            | Tipo de publicación equivocada |
| P, Warde and M, Mason and K, Ding and P, Kirkbride and M, Brundage and R, Cowan and M, Gospodarowicz and K, Sanders and E, Kostashuk and G, Swanson and J, Barber and A, Hiltz and MK, Parmar and J, Sathya and J, Anderson and C, Hayter and J, Hetherington and MR, Sydes and W, Parulekar | Combined androgen deprivation therapy and radiation therapy for locally advanced prostate cancer: a randomised, phase 3 trial.                                                                                                                                | Lancet (London, England)                                   | 2011 | 378     | 9809   | 2104-2111  | Comparación equivocada         |
| KK, Ternov and Sønksen, J and Fode, M and Lindberg, H and Kistorp, C and Bisbjerg, R and Faber, J and TW, Klausen and Palapattu, G and PB, Østergren                                                                                                                                         | Fatigue, health-related quality-of-life and metabolic changes in men treated with enzalutamide or abiraterone acetate plus prednisone for metastatic castration-resistant prostate cancer: A randomised clinical trial (HEAT). PG - 75-84 LID - S0959-8049(22 |                                                            |      |         | 1879   |            | Tipo de publicación equivocada |
| Chi, K N and Chowdhury, S and Bjartell, A and Chung, B H and De Santana Gomes, A J P and Given, R and Soto, A J and Merseburger, A S and                                                                                                                                                     | Final analysis results from TITAN: a phase III study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) receiving androgen deprivation therapy (ADT)                                    | Journal of clinical oncology                               | 2021 | 39      | 6      |            | Tipo de publicación equivocada |

| Autor                                                                                                                                                                     | Título                                                                                                                                                                                                                                                          | Revista                                                                                                                                                     | Año  | Volumen | Número | Páginas | Razón de exclusión             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|------|---------|--------|---------|--------------------------------|
| Ozguroglu, M and Uemura, H and al., et                                                                                                                                    |                                                                                                                                                                                                                                                                 |                                                                                                                                                             |      |         |        |         |                                |
| Smith, M R and Saad, F and Rathkopf, D E and Hadaschik, B A and Chowdhury, S and Yu, M K and Lopez-Gitlitz, A and Rooney, O B and Darif, M and Small, E J                 | Relationship of time to metastasis (TTM) and site of metastases in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC): Results from the phase 3 SPARTAN trial                                                                      | Journal of Clinical Oncology                                                                                                                                | 2018 | 36      | 15     |         | Tipo de publicación equivocada |
| EUCTR2012-002940-26-SE                                                                                                                                                    | A Study of Abiraterone Acetate and Prednisone with Androgen Deprivation Therapy (ADT) compared to ADT Alone in men newly Diagnosed (within the previous 3 months) with High-Risk, Metastatic (spread of cancer cells from one part of the body to another) Horm | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2012-002940-26-SE">https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2012-002940-26-SE</a> | 2012 |         |        |         | Tipo de publicación equivocada |
| NL-OMON46876                                                                                                                                                              | A Randomized, Double Blind, Multicenter, Parallel-group, Phase III study to evaluate efficacy and safety of DCVAC/PCa versus Placebo in Men with metastatic Castration Resistant Prostate Cancer eligible for 1st line chemotherapy                             | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=NL-OMON46876">https://trialsearch.who.int/Trial2.aspx?TrialID=NL-OMON46876</a>                     | 2013 |         |        |         | Tipo de publicación equivocada |
| CTIS2022-502373-42-00                                                                                                                                                     | Metastasis-directed therapy, whether or not in combination with hormone therapy, in patients with prostate cancer recurrence after initial treatment and a maximum of 5 metastases                                                                              | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=CTIS2022-502373-42-00">https://trialsearch.who.int/Trial2.aspx?TrialID=CTIS2022-502373-42-00</a>   | 2023 |         |        |         | Tipo de publicación equivocada |
| Freedland, S J and Gleave, M and De Giorgi, U and Rannikko, A and Pieczonka, C M and Tutrone, R F and Venugopal, B and Woo, H and Backhaus, M R and Supiot, S and al., et | LONGITUDINAL CHANGES IN PATIENT-REPORTED OUTCOMES (PROs) IN PATIENTS WITH HIGH-RISK BIOCHEMICALLY RECURRENT (BCR) NONMETASTATIC CASTRATION-SENSITIVE PROSTATE CANCER (NMCSPC) FROM THE EMBARK STUDY                                                             | Urologic oncology: seminars and original investigations                                                                                                     | 2024 | 42      |        | S18-S18 | Tipo de publicación equivocada |
| Khalaf, D and Sunderland, K and Eigl, B J and Finch, D L and Oja, C D and Vergidis, J and Parimi, S and Zulfikar, M and Gleave, M and Chi, K N                            | Assessment of quality of life (QOL), cognitive function and depression in a randomized phase II study of abiraterone acetate (ABI) plus prednisone (P) vs enzalutamide (ENZA) for metastatic castrate-resistant prostate cancer (mCRPC)                         | Journal of clinical oncology                                                                                                                                | 2017 | 35      | 15     |         | Tipo de publicación equivocada |
| De Souza, P and Smith, M R and Fizazi, K and Saad, F and Mulders, P F A and Sternberg,                                                                                    | Final analysis of the randomised, phase 3, COU-AA-302 study of abiraterone acetate (AA) in chemotherapy-naïve patients with                                                                                                                                     | BJU international                                                                                                                                           | 2015 | 115     |        | 21-22   | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                          | Título                                                                                                                                                                                                      | Revista                                                     | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| C N and Miller, K and Logothetis, C J and Shore, N and Small, E J and al., et                                                                                                                                                                                  | metastatic castration-resistant prostate cancer (mCRPC)                                                                                                                                                     |                                                             |      |         |        |         |                                |
| S, Chowdhury and S, Oudard and H, Uemura and S, Joniau and L, Dearden and C, Capone and S, Van Sanden and J, Diels and BA, Hadaschik                                                                                                                           | Apalutamide Compared with Darolutamide for the Treatment of Non-metastatic Castration-Resistant Prostate Cancer: Efficacy and Tolerability in a Matching-Adjusted Indirect Comparison.                      | Advances in therapy                                         | 2022 | 39      | 1      | 518-531 | Diseño de estudio equivocado   |
| Arroyo-Rojas, Y and Rodriguez-Sanchez, L and Colandrea, G and Otaola Arca, H and Lanz, C and Barret, E and Sanchez-Salas, R and Macek, P and Cathelineau, X                                                                                                    | The role of androgen deprivation therapy prior to radical prostatectomy in high-risk prostate cancer: a systematic review                                                                                   | Minerva Urology and Nephrology                              | 2024 | 76      | 2      | 141-147 | Tratamiento equivocado         |
| Cardili, Leonardo and Bastos, Diogo Assed and Ilario, Eder Nisi and Pereira, Marina Alessandra and Guglielmetti, Giuliano Bettoni and Cordeiro, Maurício and Pontes, José and Coelho, Rafael Ferreira and Nahas, William Carlos and Leite, Katia Ramos Moreira | Tumor regression after neoadjuvant hormonal therapy in high risk prostate cancer: pathological outcomes from a randomized phase II trial.                                                                   | World J Urol                                                | 2024 | 42      | 1      | 618-618 | Tratamiento equivocado         |
| A, Ramos-Esquivel and E, Garita-Rojas and A, Masis-Marroquín                                                                                                                                                                                                   | A systematic review and meta-analysis on overall survival, failure-free survival and safety outcomes in patients with metastatic hormone-sensitive prostate cancer treated with new anti-androgens.         | Anti-cancer drugs                                           | 2023 | 34      | 3      | 405-412 | No se encuentra texto completo |
| Roy, S and Malone, S and Sun, Y and Wallis, C J D and Kishan, A U and Morgan, S C and Gebrael, G and Swami, U and Jia, A and Brown, J R and al., et                                                                                                            | Differential treatment effect on overall survival (OS) based on early prostate-specific antigen (PSA) response in metastatic hormone-sensitive prostate cancer (mHSPC): a secondary analysis of TITAN trial | Journal of clinical oncology                                | 2024 | 42      | 4      |         | Tipo de publicación equivocada |
| Nabid, A and Carrier, N and Vigneault, E and Souhami, L and Lemaire, C and Brassard, M A and Bahoric, B and Archambault, R and Vincent, F and Nguyen, T V                                                                                                      | Radiation therapy with or without short-term androgen deprivation therapy in intermediate-risk prostate cancer: results of a phase 3 trial                                                                  | International journal of radiation oncology biology physics | 2016 | 94      | 1      | 4-4     | Tipo de publicación equivocada |
| T, Iguchi and S, Tamada and M, Kato and S, Yasuda and Y,                                                                                                                                                                                                       | Enzalutamide versus flutamide for castration-resistant prostate cancer after combined                                                                                                                       | International journal of clinical oncology                  | 2020 | 25      | 3      | 486-494 | No se encuentra                |

| Autor                                                                                                                                                                                                                   | Título                                                                                                                                                                                                                                        | Revista                                                                                                                                                   | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|------|---------|--------|-------------|--------------------------------|
| Machida and T, Ohmachi and K, Ishii and H, Iwata and S, Yamamoto and T, Kanamaru and K, Morimoto and T, Hase and K, Tashiro and K, Harimoto and T, Deguchi and T, Adachi and K, Iwamoto and Y, Takegaki and T, Nakatani | androgen blockade therapy with bicalutamide: the OCUU-CRPC study.                                                                                                                                                                             |                                                                                                                                                           |      |         |        |             | texto completo                 |
| ChiCTR-TRC-10001866                                                                                                                                                                                                     | A comparative study of two adjuvant hormone therapy regimens in high-risk prostate cancer after radical prostatectomy: maximum androgen blockade with medical/surgical castration and bicalutamide 50mg                                       | <a href="https://trialsearch.world.int/Trial2.aspx?TrialID=ChiCTR-TRC-10001866">https://trialsearch.world.int/Trial2.aspx?TrialID=ChiCTR-TRC-10001866</a> | 2010 |         |        |             | Tipo de publicación equivocada |
| Attard, G and Borre, M and Gurney, H and Lortot, Y and Andresen, C and Kallada, R and Pham, T and Taplin, M.-E.                                                                                                         | A phase IV, randomized, double-blind, placebo (PBO)-controlled study of continued enzalutamide (ENZA) post prostate-specific antigen (PSA) progression in men with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC) | Journal of Clinical Oncology                                                                                                                              | 2017 | 35      | 15     |             | Tipo de publicación equivocada |
| Sabran, M Z and Wibisono, M G and Wibisono, M H H and Li, C.-Y. and Liao, S.-Y. and Wibisono, J J and Kurniawan, A and Huang, I                                                                                         | Patients health-related quality of life in men with prostate cancer treated by enzalutamide: A systematic review                                                                                                                              | Annals of Oncology                                                                                                                                        | 2024 | 35      |        | S1542-S1542 | Tipo de publicación equivocada |
| Smith, M R and Klotz, L and Persson, B E and Olesen, T K and Wilde, A A                                                                                                                                                 | Cardiovascular safety of degarelix: results from a 12-month, comparative, randomized, open label, parallel group phase III trial in patients with prostate cancer                                                                             | Journal of urology                                                                                                                                        | 2010 | 184     | 6      | 2313-2319   | Tratamiento equivocado         |
| Izumi, K and Nakagawa, R and Mizokami, A                                                                                                                                                                                | Enzalutamide vs abiraterone plus prednisolone for elderly CRPC patients: From the ENABLE phase III trial                                                                                                                                      | Annals of Oncology                                                                                                                                        | 2024 | 35      |        | S1536-S1536 | Tipo de publicación equivocada |
| Matveev, V and Gao, X and Kopyltsov, E and Luo, J and Wei, Q and Ye, D and Zhou, F and Cabri, P and Houchard, A and Mahmood, A and al., et                                                                              | PRIORITI: phase 4 study of triptorelin or active surveillance in high-risk prostate cancer                                                                                                                                                    | Asia-Pacific journal of clinical oncology                                                                                                                 | 2024 | 20      | 6      | 738-746     | Tratamiento equivocado         |
| Risson, V and Maheshwari, V and Chakravarty, A and O'Loughlin, A and Khare, A and Joshi, P                                                                                                                              | Comparison of Survival Outcomes for [177Lu]Lu-PSMA-617 vs Other Systemic Treatments in Post-Taxane Metastatic Castration-Resistant Prostate Cancer Setting: A Bayesian Network Meta-Analysis                                                  | Value in Health                                                                                                                                           | 2024 | 27      | 12     | S22-S23     | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                      | Título                                                                                                                                                                                                                                                                          | Revista                                                                                                                             | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|------|---------|--------|-----------|--------------------------------|
| Latorzeff, I and Guerif, S and Castan, F and Meyer, E and Supiot, S and Lagneau, E and Deniaud-Alexandre, E and Ronchin, P and Benyoucef, A and Cartier, L and al., et                     | GETUG-AFU 22 phase II randomized trial : final results on clinical outcomes with immediate SRT                                                                                                                                                                                  | Radiotherapy and oncology                                                                                                           | 2023 | 182     |        | S334-S334 | Tipo de publicación equivocada |
| Aziz, M and Molony, D and Monlezun, D and Higgason, N and Brunckhorst, O and Roland, J and Owen, C and Iacobucci, A S and Galan, J and Swaby, J and Deng, B and Hartshorne, T and Desai, S | A Systematic Review and Network Meta-Analysis of Metastatic CastrateResistant Prostate Cancer Therapy Cardiotoxicity Given Metastatic Hormone-Sensitive Prostate Cancer Treatment History                                                                                       | Circulation                                                                                                                         | 2024 | 150     |        |           | Tipo de publicación equivocada |
| CTIS2022-501343-33-00                                                                                                                                                                      | A study to compare the study treatment darolutamide in combination with androgen deprivation therapy (ADT) to placebo in combination with ADT in men with elevated blood levels of a specific protein called PSA, which is a marker for high-risk of prostate cancer recurrence |                                                                                                                                     | 2023 |         |        |           | Tipo de publicación equivocada |
| Shore, N D and Hussain, M and Saad, F and Fizazi, K and Sternberg, C N and Crawford, D and Tombal, B and Nordquist, L and Cookson, M and Verholen, F and al., et                           | Efficacy and Safety of Darolutamide in Combination With Androgen-Deprivation Therapy and Docetaxel in Black Patients From the Randomized ARASENS Trial                                                                                                                          | Oncologist                                                                                                                          | 2024 | 29      | 3      | 235-243   | Tratamiento equivocado         |
| Saad, F and Thiery-Vuillemin, A and Wiechno, P and Alekseev, B and Sala, N and Jones, R and Kocak, I and Chiuri, V E and Jassem, J and Flechon, A and al., et                              | Patient-reported outcomes with olaparib plus abiraterone versus placebo plus abiraterone for metastatic castration-resistant prostate cancer: a randomised, double-blind, phase 2 trial                                                                                         | The lancet. Oncology                                                                                                                | 2022 | 23      | 10     | 1297-1307 | Tratamiento equivocado         |
| Aizawa, R and Ishikawa, H and Kato, M and Shimizu, S and Mizowaki, T and Kohjimoto, Y and Hinotsu, S and Hara, I                                                                           | Significance of androgen-deprivation therapy for intermediate- and high-risk prostate cancer treated with high-dose radiotherapy: A literature review                                                                                                                           | International Journal of Urology                                                                                                    | 2024 | 31      | 10     | 1068-1079 | Comparación equivocada         |
| PER-110-20                                                                                                                                                                                 | PHASE 3 STUDY OF DAROLUTAMIDE IN ADDITION TO ADT VERSUS PLACEBO PLUS ADT IN MEN WITH MHSPC                                                                                                                                                                                      | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=PER-110-20">https://trialsearch.who.int/Trial2.aspx?TrialID=PER-110-20</a> | 2021 |         |        |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                      | Título                                                                                                                                                                                                                                                         | Revista                                                                                                                                                     | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Liau, R and Sutanto, R and Subrata, J A K                                                                                                                                                  | Safety and efficacy of olaparib in metastatic castration-resistant prostate cancer with DNA damage repair aberrations                                                                                                                                          | Annals of Oncology                                                                                                                                          | 2024 | 35      |        | S1399-S1400 | Tipo de publicación equivocada |
| V, Grünwald and CH, Ohlmann and B, Hadaschik                                                                                                                                               | Re: Abiraterone Acetate and Prednisolone With or Without Enzalutamide for High-risk Non-metastatic Prostate Cancer: A Meta-analysis of Primary Results from Two Randomized Controlled Phase 3 Trials of the STAMPEDE Platform Protocol.                        | European urology                                                                                                                                            | 2022 | 81      | 6      | 621-621     | Tipo de publicación equivocada |
| UMIN000002822                                                                                                                                                                              | Pilot study for randomized clinical trial of bicalutamide alone versus bicalutamide plus goserelin acetate in patients with PSA failure after radical prostatectomy                                                                                            | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=JPRN-UMIN000002822">https://trialsearch.who.int/Trial2.aspx?TrialID=JPRN-UMIN000002822</a>         | 2009 |         |        |             | Tipo de publicación equivocada |
| Shelan, M and Achard, V and Appiagyei, F and Mose, L and Zilli, T and Fankhauser, C D and Zamboglou, C and Mohamad, O and Aebbersold, D M and Cathomas, R                                  | Role of enzalutamide in primary and recurrent non-metastatic hormone sensitive prostate cancer: a systematic review of prospective clinical trials                                                                                                             | Prostate Cancer and Prostatic Diseases                                                                                                                      | 2024 | 27      | 3      | 422-431     | Población equivocada           |
| Bahl, A and Challapalli, A and Greenwood, R and Hurley, K and Persad, R                                                                                                                    | Quality of life evaluation of the effect of decapeptyl compared with zoladex preradiotherapy: final results of randomised controlled trial                                                                                                                     | Journal of clinical oncology                                                                                                                                | 2017 | 35      | 6      |             | Tipo de publicación equivocada |
| Guerif, S G and Latorzeff, I and Roca, L and Allouache, D and Supiot, S and Lagneau, E and Richaud, P and Elisabeth, D-A and Ronchin, P and Ahmed, B and al., et                           | The acute toxicity results of the GETUG-AFU 22 study: a multicenter randomized phase II trial comparing the efficacy of a short hormone therapy in combination with radiotherapy to radiotherapy alone as a salvage treatment for patients with detectable PSA | Journal of clinical oncology                                                                                                                                | 2017 | 35      | 6      |             | Tipo de publicación equivocada |
| EUCTR2010-022037-29-FR                                                                                                                                                                     | Phase III randomised trial to evaluate the benefit of adjuvant hormonal treatment with leuporelin acetate (Eligard® 45 mg) for 24 months after radical prostatectomy in patients with high risk of recurrence                                                  | <a href="https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2010-022037-29-FR">https://trialsearch.who.int/Trial2.aspx?TrialID=EUCTR2010-022037-29-FR</a> | 2010 |         |        |             | Tipo de publicación equivocada |
| S, Chowdhury and S, Oudard and H, Uemura and S, Joniau and D, Pilon and M, Ladouceur and AS, Behl and J, Liu and L, Dearden and J, Sermon and S, Van Sanden and J, Diels and BA, Hadaschik | Matching-Adjusted Indirect Comparison of the Efficacy of Apalutamide and Enzalutamide with ADT in the Treatment of Non-Metastatic Castration-Resistant Prostate Cancer.                                                                                        | Advances in therapy                                                                                                                                         | 2020 | 37      | 1      | 501-511     | Diseño de estudio equivocado   |

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| SJ, Freedland and M, Gleave and U, De Giorgi and A, Rannikko and CM, Pieczonka and RF, Tutrone and B, Venugopal and HH, Woo and M, Ramirez-Backhaus and S, Supiot and A, Lantz and A, Ganguli and J, Ivanova and P, Kral and SP, Huang and F, Saad and ND, Shore | Enzalutamide and Quality of Life in Biochemically Recurrent Prostate Cancer.                                                                                                                                                                                                                                 | NEJM evidence                                               | 2023 | 2       | 12     | EVIDoa2300251-EVIDoa2300251 | Tipo de publicación equivocada |
| A, Sciarra and A, Fasulo and A, Ciardi and E, Petrangeli and A, Gentilucci and M, Maggi and M, Innocenzi and F, Pierella and V, Gentile and S, Salciccia and S, Cattarino                                                                                        | A meta-analysis and systematic review of randomized controlled trials with degarelix versus gonadotropin-releasing hormone agonists for advanced prostate cancer.                                                                                                                                            | Medicine                                                    | 2016 | 95      | 27     | e3845-e3845                 | Comparación equivocada         |
| Huang, Y and Gu, D and He, H and Liang, L and Zhang, Y and Zhang, Q and Peng, K and Wang, Y and Wu, J and Long, X                                                                                                                                                | PARP Inhibitor for the Treatment of Prostatic Cancer: A Systematic Review and Network Meta-Analysis                                                                                                                                                                                                          | Journal of Endourology                                      | 2024 | 38      |        | A18-A19                     | Tipo de publicación equivocada |
|                                                                                                                                                                                                                                                                  | A Multinational, Multicenter, Prospective, Randomized, Controlled, Open-Label, Phase 3 Study of Lutetium (177Lu) Rosopatomab Tetraxetan in Combination With Standard of Care Versus Standard of Care Alone in Patients With PSMA Positive Metastatic Castration-Resistant Prostate Cancer Previously Afte... | <a href="https://clinicaltrials.gov">clinicaltrials.gov</a> | 2024 |         |        |                             | Tipo de publicación equivocada |
|                                                                                                                                                                                                                                                                  | A Randomized Phase III Trial Evaluating the Efficacy and Safety of Standard of Care +/- 177Lu-PSMA617 in de Novo Metastatic Hormone-sensitive Prostate Cancer Patients Having a PSA≥0.2 ng/mL at 6-8 Months After Systemic Treatment Initiation                                                              | <a href="https://clinicaltrials.gov">clinicaltrials.gov</a> | 2024 |         |        |                             | Tipo de publicación equivocada |
| Matsukawa, A and Rajwa, P and Kawada, T and Bekku, K and Laukhtina, E and Klemm, J and Pradere, B and Mori, K and Karakiewicz, P I and Kimura, T and Chlosta, P and                                                                                              | Impact of disease volume on survival efficacy of triplet therapy for metastatic hormone-sensitive prostate cancer: a systematic review, meta-analysis, and network meta-analysis                                                                                                                             | International Journal of Clinical Oncology                  | 2024 | 29      | 6      | 716-725                     | Desenlace equivocado           |

| Autor                                                                                                                                                                                                                                                                                                                            | Título                                                                                                                                                                                                                   | Revista                      | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| Shariat, S F and Yanagisawa, T                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                          |                              |      |         |        |         |                                |
| Chen, L and Chen, Z and Liang, X and Xuan, J                                                                                                                                                                                                                                                                                     | A Systematic Literature Review of Comparative Efficacy Measures in Randomized Controlled Trials of Darolutamide Treatment in Metastatic Hormone-Sensitive Prostate Cancer                                                | Value in Health              | 2024 | 27      | 6      | S24-S24 | Tipo de publicación equivocada |
| MV, Pilepich and Caplan R FAU - Byhardt, R W and Byhardt RW FAU - Lawton, C A and Lawton CA FAU - Gallagher, M J and Gallagher MJ FAU - Mesic, J B and Mesic JB FAU - Hanks, G E and Hanks GE FAU - Coughlin, C T and Coughlin CT FAU - Porter, A and Porter A FAU - Shipley, W U and Shipley WU FAU - Grignon, D and Grignon, D | Phase III trial of androgen suppression using goserelin in unfavorable-prognosis carcinoma of the prostate treated with definitive radiotherapy: report of Radiation Therapy Oncology Group Protocol 85-31. PG - 1013-21 |                              |      |         | 732    |         | Tipo de publicación equivocada |
| Holzgrevé, A and Delker, A and Ells, Z and Brosch-Lenz, J and Zhu, S and Lira, S and Nikitas, J and Grogan, T and Elashoff, D and Unterrainer, L M and Dahlbom, M and Allen-Auerbach, M S and Czernin, J and Calais, J                                                                                                           | A randomized phase 2 trial in progress of flexible and extended dosing of 177Lu-PSMA-617 molecular radioligand therapy in mCRPC (FLEX-MRT)                                                                               | Journal of Clinical Oncology | 2024 | 42      | 16     |         | Tipo de publicación equivocada |
| Manikandan, R and Srirangam SJ FAU - Pearson, Evelyn and Pearson E FAU - Brown, Stephen C W and Brown SC FAU - O'Reilly, Patrick and O'Reilly P FAU - Collins, Gerald N and GN, Collins                                                                                                                                          | Diethylstilboestrol versus bicalutamide in hormone refractory prostate carcinoma: a prospective randomized trial. PG - 217-21                                                                                            |                              |      |         | 42     |         | Tipo de publicación equivocada |
| Jacobo, E and Schmidt, J D and Weinstein, S H and Flocks, R H                                                                                                                                                                                                                                                                    | Comparison of flutamide (SCH-13521) and diethylstilbestrol in untreated advanced prostatic cancer                                                                                                                        | Urology                      | 1976 | 8       | 3      | 231-233 | Comparación equivocada         |
| Garnick, M B                                                                                                                                                                                                                                                                                                                     | Leuprolide versus diethylstilbestrol for previously untreated stage D2 prostate cancer. Results of a prospectively randomized trial                                                                                      | Urology                      | 1986 | 27      | 1      | 21-28   | Comparación equivocada         |



| Autor                                                                                                                                                                                                                                                                              | Título                                                                                                                                                                                                                 | Revista                                                                                               | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Moffat, L E                                                                                                                                                                                                                                                                        | Comparison of Zoladex, diethylstilbestrol and cyproterone acetate treatment in advanced prostate cancer                                                                                                                | European urology                                                                                      | 1990 | 18      |        | 26-27       | Comparación equivocada         |
| NCT00002597                                                                                                                                                                                                                                                                        | Radiation Therapy With or Without Antiandrogen Therapy in Treating Patients With Stage I or Stage II Prostate Cancer                                                                                                   | <a href="https://clinicaltrials.gov/show/NCT00002597">https://clinicaltrials.gov/show/NCT00002597</a> | 1999 |         |        |             | Tipo de publicación equivocada |
| Gravis, G and Boher, J M and Joly, F and Soulié, M and Albiges, L and Priou, F and Latorzeff, I and Delva, R and Krakowski, I and Laguerre, B and al., et                                                                                                                          | Androgen Deprivation Therapy (ADT) Plus Docetaxel Versus ADT Alone in Metastatic Non castrate Prostate Cancer: impact of Metastatic Burden and Long-term Survival Analysis of the Randomized Phase 3 GETUG-AFU15 Trial | European urology                                                                                      | 2016 | 70      | 2      | 256-262     | Tratamiento equivocado         |
| Lund, F and Rasmussen, F                                                                                                                                                                                                                                                           | Flutamide versus stilboestrol in the management of advanced prostatic cancer. A controlled prospective study. PG - 140-2                                                                                               |                                                                                                       |      |         | 7      |             | Tipo de publicación equivocada |
| See, W A and Wirth, M P and McLeod, D G and Iversen, P and Klimberg, I and Gleason, D and Chodak, G and Montie, J and Tyrrell, C and Wallace, D M A and Delaere, K P J and Vaage, S and Tammela, T L J and Lukkarinen, O and Persson, B.-E. and Carroll, K and Kolvenbag, G.J.C.M. | Bicalutamide as immediate therapy either alone or as adjuvant to standard care of patients with localized or locally advanced prostate cancer: First analysis of the early prostate cancer program                     | Journal of Urology                                                                                    | 2002 | 168     | 2      | 429-435     | Tratamiento equivocado         |
| Devos, G T and Tosco, L and Baldewijns, M and Giesen, A and Gevaert, T and Goffin, K and Petit, V and Mai, C and Raskin, Y and Van Haute, C and De Meerleer, G and Berghen, C and Devlies, W and Van Poppel, H and Claessens, F and Everaerts, W and Joniau, S                     | Three-year oncological outcomes of the randomized phase II trial ARNEO: Neoadjuvant degarelix with or without apalutamide prior to radical prostatectomy for high-risk prostate cancer                                 | European Urology                                                                                      | 2024 | 85      |        | S1514-S1514 | Tipo de publicación equivocada |
| NCT00651326                                                                                                                                                                                                                                                                        | Androgen Suppression and Radiation With/Out Docetaxel in High-Risk Localized Prostate Cancer                                                                                                                           | <a href="https://clinicaltrials.gov/show/NCT00651326">https://clinicaltrials.gov/show/NCT00651326</a> | 2008 |         |        |             | Tipo de publicación equivocada |
| Carvalho, A P and de Moura, J L and Denis, L and Newling, D and Smith, P and Bono, A and                                                                                                                                                                                           | Zoladex and flutamide vs orchidectomy: a phase III EORTC 30853 trial. EORTC Urological Group                                                                                                                           | Progress in clinical and biological research                                                          | 1989 | 303     |        | 129-143     | Tratamiento equivocado         |

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| Sylvester, R and De Pauw, M and Ongena, P                                                                                                                                                                                                                                    |                                                                                                                                                                                                   |                                       |      |         |        |                   |                                |
| D'Amico, A V and Xie, W and McMahon, E and Loffredo, M and Medeiros, S and Joseph, D J and Denham, J W and Lamb, D S and Kumar, P and Buble, G and Sullivan, M A and Hellwig, R and Vera, J C and Freter, R and Baker, W J and Wong, J Y C and Renshaw, A A and Kantoff, P W | Radiation and androgen deprivation therapy with or without docetaxel in the management of non-metastatic unfavorable-risk prostate cancer: A prospective randomized trial                         | Journal of Clinical Oncology          | 2021 | 39      | 15     |                   | Tratamiento equivocado         |
| Jr, Goodman O B and TW, Flaig and Molina, A and PF, Mulders and Fizazi, K and Suttman, H and Li, J and Kheoh, T and JS, de Bono and HI, Scher                                                                                                                                | Exploratory analysis of the visceral disease subgroup in a phase III study of abiraterone acetate in metastatic castration-resistant prostate cancer. PG - 34-9 LID - 10.1038/pcan.2013.41 [doi]  |                                       |      |         | 1476   |                   | Tipo de publicación equivocada |
| Soon, Y Y and Marschner, I C and Schou, M and Hofman, M S and Emmett, L and Davis, I D and Stockler, M R and Martin, A J                                                                                                                                                     | Lu-177 PSMA vs Comparator Treatments and Survival in Metastatic Castration-Resistant Prostate Cancer                                                                                              | JAMA network open                     | 2024 | 7       | 9      | e2433863-e2433863 | Diseño de estudio equivocado   |
| Kotake, T and Usami, M and Akaza, H and Koiso, K and Homma, Y and Kawabe, K and Aso, Y and Orikasa, S and Shimazaki, J and Isaka, S and Yoshida, O and Hirao, Y and Okajima, E and Naito, S and Kumazawa, J and Kanetake, H and Saito, Y and Ohi, Y and Ohashi, Y            | Goserelin acetate with or without antiandrogen or estrogen in the treatment of patients with advanced prostate cancer: a multicenter, randomized, controlled trial in Japan. Zoladex Study Group. | Japanese journal of clinical oncology | 1999 | 29      | 11     | 562-570           | Comparación equivocada         |
| Morales, R G and Naqvi, S A A and Ayaz, A and Khakwani, K Z R and Riaz, Z B and Raina, A and Ravi, P and Childs, D S and Andrews, J R and Orme, J and Cobran, E K and Singh, P and Riaz, I B and Bryce, A H                                                                  | Comparative health-related quality of life (QoL) in metastatic castration-sensitive prostate cancer (mCSPC): A living systematic review                                                           | Journal of Clinical Oncology          | 2024 | 42      | 4      |                   | Tipo de publicación equivocada |

| Autor                                                                                                                                                                               | Título                                                                                                                                                                                      | Revista                                                                                               | Año  | Volumen | Número | Páginas                      | Razón de exclusión             |
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| NCT04343885                                                                                                                                                                         | In Men With Metastatic Prostate Cancer, What is the Safety and Benefit of Lutetium-177 PSMA Radionuclide Treatment in Addition to Chemotherapy                                              | <a href="https://clinicaltrials.gov/show/NCT04343885">https://clinicaltrials.gov/show/NCT04343885</a> | 2020 |         |        |                              | Tipo de publicación equivocada |
| Naqvi, S A A and Riaz, I B and Khakwani, K Z R and Bibi, A and Andrews, J R and Childs, D S and Ravi, P and Orme, J and Singh, P and Sweeney, C and Bryce, A H                      | Comparative survival in metastatic castration-sensitive prostate cancer (mCSPC) by prognostic subgroups: A living network meta-analysis                                                     | Journal of Clinical Oncology                                                                          | 2024 | 42      | 4      |                              | Repetido                       |
| Di Silverio, F and Sciarra, F and D'Eramo, G                                                                                                                                        | Advanced prostatic cancer: clinical and hormonal response to flutamide in patients pretreated with LHRH analogue and cyproterone acetate                                                    | European urology                                                                                      | 1990 | 18      | 1      | 10-15                        | No se encuentra texto completo |
| Citrin, D L and Resnick, M I and Guinan, P and al-Bussam, N and Scott, M and Gau, T C and Kennealey, G T                                                                            | A comparison of Zoladex and DES in the treatment of advanced prostate cancer: results of a randomized, multicenter trial                                                                    | Prostate                                                                                              | 1991 | 18      | 2      | 139-146                      | Comparación equivocada         |
| Guo, X and Li, Y and Wang, M and Peng, H and Guo, H and Hou, T and Zhang, H and Jiang, J and Sheng, T and Fan, Y and Wu, T and He, Z                                                | Efficacy and safety between first-line therapies in metastatic castration-resistant prostate cancer in combination in the PARPi and ARSI era: A systematic review and network meta-analysis | Journal of Clinical Oncology                                                                          | 2024 | 42      | 4      |                              | Tipo de publicación equivocada |
| NCT03356912                                                                                                                                                                         | CABazitaxel With or Without Prednisone in Patients With Metastatic CAstration REsistant Prostate Cancer Progressed During or After a Previous Docetaxel-based Chemotherapy                  | <a href="https://clinicaltrials.gov/show/NCT03356912">https://clinicaltrials.gov/show/NCT03356912</a> | 2017 |         |        |                              | Tipo de publicación equivocada |
| Emtage, L A and Trethowan, C and Kelly, K and Arkell, D and Wallace, D M and Hughes, M and Hay, A and Blacklock, R and Jones, M and Rouse, A                                        | A phase III open randomized study of Zoladex 3.6 mg depot vs. DES 3 mg per day in untreated advanced prostate cancer: a West Midlands Urological Research Group Study                       | Progress in clinical and biological research                                                          | 1989 | 303     |        | 47-52                        | No se encuentra texto completo |
| Di Silverio, F and Serio, M and D'Eramo, G and Sciarra, F                                                                                                                           | Zoladex vs. Zoladex plus cyproterone acetate in the treatment of advanced prostatic cancer: a multicenter Italian study                                                                     | European urology                                                                                      | 1990 | 18      |        | 54-61                        | Comparación equivocada         |
| Seidenfeld, J and Samson, D J and Aronson, N and Albertson, P C and Bayoumi, A M and Bennett, C and Brown, A and Garber, A and Gere, M and Hasselblad, V and Wilt, T and Ziegler, K | Relative effectiveness and cost-effectiveness of methods of androgen suppression in the treatment of advanced prostate cancer.                                                              | Evidence report/technology assessment (Summary)                                                       | 1999 |         | 4      | i-x, 1-246, I1-24636, passim | Diseño de estudio equivocado   |

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| NCT02918968                                                                                                                                                                                   | Study on Enzalutamide and Flutamide in Patients With Castration Resistant Prostate Cancer                                                                                                                                                           | <a href="https://clinicaltrials.gov/ct2/show/NCT02918968">https://clinicaltrials.gov/ct2/show/NCT02918968</a> | 2016 |         |        |           | Tipo de publicación equivocada |
| NCT00002633                                                                                                                                                                                   | Hormone Therapy With or Without Surgery or Radiation Therapy in Treating Patients With Prostate Cancer                                                                                                                                              | <a href="https://clinicaltrials.gov/show/NCT00002633">https://clinicaltrials.gov/show/NCT00002633</a>         | 1999 |         |        |           | Tipo de publicación equivocada |
| Usami, M and Kotake, T and Matsuda, M and Okajima, E and Osafune, M and Aso, Y and Ishigami, J and Itatani, H and Ohi, Y and Ohkawa, T                                                        | Treatment of prostatic carcinoma with daily subcutaneous injection of the LH-RH analogue, ICI 118630                                                                                                                                                | Hinyokika kiyo. Acta urologica Japonica                                                                       | 1986 | 32      | 10     | 1475-1488 | Diseño de estudio equivocado   |
| NCT02485691                                                                                                                                                                                   | Cabazitaxel Versus the Switch to Alternative AR-targeted Agent (Enzalutamide or Abiraterone) in Metastatic Castration-resistant Prostate Cancer (mCRPC) Patients Previously Treated With Docetaxel and Who Rapidly Failed a Prior AR-targeted Agent | <a href="https://clinicaltrials.gov/show/NCT02485691">https://clinicaltrials.gov/show/NCT02485691</a>         | 2015 |         |        |           | Tipo de publicación equivocada |
| NCT06894511                                                                                                                                                                                   | An Open-label Study Comparing Lutetium (177Lu) Vipivotide Tetraxetan in Combination With ARPI Versus AAA617 in PSMA Positive First-line mCRPC                                                                                                       | <a href="https://clinicaltrials.gov/ct2/show/NCT06894511">https://clinicaltrials.gov/ct2/show/NCT06894511</a> | 2025 |         |        |           | Tipo de publicación equivocada |
| T, Jiang and D, Markovic and J, Patel and JE, Juarez and TM, Ma and D, Shabsovich and NG, Nickols and RE, Reiter and D, Elashoff and MB, Rettig and NG, Zaorsky and DE, Spratt and AU, Kishan | Radiation therapy dose and androgen deprivation therapy in localized prostate cancer: a meta-regression of 5-year outcomes in phase III randomized controlled trials.                                                                               | Prostate cancer and prostatic diseases                                                                        | 2022 | 25      | 1      | 126-128   | Desenlace equivocado           |
| Jiang, J and Wang, Y and Bai, J and Yang, G and Wang, H and Ding, H and Zhang, Y and Zhai, Z and Dong, Z and Wang, Z                                                                          | Efficacy and safety of triple or dual therapies for metastatic hormone-sensitive prostate cancer: a systematic review and Bayesian network meta-analysis                                                                                            | Future Oncology                                                                                               | 2024 |         |        |           | Tipo de publicación equivocada |
| NCT01308567                                                                                                                                                                                   | Cabazitaxel Versus Docetaxel Both With Prednisone in Patients With Metastatic Castration Resistant Prostate Cancer                                                                                                                                  | <a href="https://clinicaltrials.gov/show/NCT01308567">https://clinicaltrials.gov/show/NCT01308567</a>         | 2011 |         |        |           | Tipo de publicación equivocada |
| K, Fizazi and HI, Scher and A, Molina and CJ, Logothetis and KN, Chi and RJ, Jones and JN, Staffurth and S, North and NJ, Vogelzang and F, Saad and P, Mainwaring and S, Harland              | Abiraterone acetate for treatment of metastatic castration-resistant prostate cancer: final overall survival analysis of the COU-AA-301 randomised, double-blind, placebo-controlled phase 3 study.                                                 | The Lancet. Oncology                                                                                          | 2012 | 13      | 10     | 983-992   | Comparación equivocada         |

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| and Jr, Goodman O B and CN, Sternberg and JH, Li and T, Kheoh and CM, Haqq and de Bono JS                                                               |                                                                                                                                                                                                                            |                                                                                                               |      |         |        |         |                                |
| NCT02582749                                                                                                                                             | Androgen Deprivation Therapy +/- Radium-223 Dichloride in Metastatic Prostate Cancer With Bone Metastases                                                                                                                  | <a href="https://clinicaltrials.gov/show/NCT02582749">https://clinicaltrials.gov/show/NCT02582749</a>         | 2015 |         |        |         | Tipo de publicación equivocada |
| NCT02199197                                                                                                                                             | Radium Ra 223 With Enzalutamide Compared to Enzalutamide Alone in Men With Metastatic Castration Refractory Prostate Cancer                                                                                                | <a href="https://clinicaltrials.gov/show/NCT02199197">https://clinicaltrials.gov/show/NCT02199197</a>         | 2014 |         |        |         | Tipo de publicación equivocada |
| NCT01576029                                                                                                                                             | Continued Treatment With Docetaxel Versus Switch to Cabazitaxel After Minor Prostate Specific Antigen Response to Docetaxel in Patients With Castration-Resistant Metastatic Prostate Cancer                               | <a href="https://clinicaltrials.gov/show/NCT01576029">https://clinicaltrials.gov/show/NCT01576029</a>         | 2012 |         |        |         | Tipo de publicación equivocada |
| M, Abufaraj and T, Iwata and S, Kimura and A, Haddad and H, Al-Ani and L, Abusubaih and M, Moschini and A, Briganti and PI, Karakiewicz and SF, Shariat | Differential Impact of Gonadotropin-releasing Hormone Antagonist Versus Agonist on Clinical Safety and Oncologic Outcomes on Patients with Metastatic Prostate Cancer: A Meta-analysis of Randomized Controlled Trials.    | European urology                                                                                              | 2021 | 79      | 1      | 44-53   | Comparación equivocada         |
| NCT02294461                                                                                                                                             | An Asian Study to Evaluate Efficacy and Safety of Oral Enzalutamide in Progressive Metastatic Prostate Cancer Participants                                                                                                 | <a href="https://clinicaltrials.gov/ct2/show/NCT02294461">https://clinicaltrials.gov/ct2/show/NCT02294461</a> | 2014 |         |        |         | Tipo de publicación equivocada |
| NCT00657904                                                                                                                                             | Bicalutamide (Casodex™) Versus Placebo in Patients With Early Prostate Cancer                                                                                                                                              | <a href="https://clinicaltrials.gov/show/NCT00657904">https://clinicaltrials.gov/show/NCT00657904</a>         | 2008 |         |        |         | Tipo de publicación equivocada |
| P, Iversen and JE, Johansson and P, Lodding and T, Kylvälä and P, Lundmo and P, Klarskov and TL, Tammela and I, Tasdemir and T, Morris and J, Armstrong | Bicalutamide 150 mg in addition to standard care for patients with early non-metastatic prostate cancer: updated results from the Scandinavian Prostate Cancer Group-6 Study after a median follow-up period of 7.1 years. | Scandinavian journal of urology and nephrology                                                                | 2006 | 40      | 6      | 441-452 | Tratamiento equivocado         |
| NCT02023697                                                                                                                                             | Standard Dose Versus High Dose and Versus Extended Standard Dose Radium-223 Dichloride in Castration-resistant Prostate Cancer Metastatic to the Bone                                                                      | <a href="https://clinicaltrials.gov/show/NCT02023697">https://clinicaltrials.gov/show/NCT02023697</a>         | 2013 |         |        |         | Tipo de publicación equivocada |
| NCT04419402                                                                                                                                             | Enzalutamide With Lu PSMA-617 Versus Enzalutamide Alone in Men With Metastatic Castration-resistant Prostate Cancer                                                                                                        | <a href="https://clinicaltrials.gov/ct2/show/NCT04419402">https://clinicaltrials.gov/ct2/show/NCT04419402</a> | 2020 |         |        |         | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                            | Título                                                                                                                                                                                                                 | Revista                                                                                                       | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| NCT01972217                                                                                                                                                                                                      | Ph II Study to Evaluate Olaparib With Abiraterone in Treating Metastatic Castration Resistant Prostate Cancer                                                                                                          | <a href="https://clinicaltrials.gov/show/NCT01972217">https://clinicaltrials.gov/show/NCT01972217</a>         | 2013 |         |        |         | Tipo de publicación equivocada |
| B, Tombal and K, Miller and L, Boccon-Gibod and F, Schröder and N, Shore and ED, Crawford and J, Moul and JK, Jensen and T, Kold Olesen and BE, Persson                                                          | Additional analysis of the secondary end point of biochemical recurrence rate in a phase 3 trial (CS21) comparing degarelix 80 mg versus leuprolide in prostate cancer patients segmented by baseline characteristics. | European urology                                                                                              | 2010 | 57      | 5      | 836-842 | Tratamiento equivocado         |
| NCT00819247                                                                                                                                                                                                      | The Efficacy and Safety of FE 200486 in Treatment of Patients Suffering From Prostate Cancer                                                                                                                           | <a href="https://clinicaltrials.gov/show/NCT00819247">https://clinicaltrials.gov/show/NCT00819247</a>         | 2009 |         |        |         | Tipo de publicación equivocada |
| NCT00673205                                                                                                                                                                                                      | (Bicalutamide) Casodex vs Placebo in Non-metastatic Early Prostate Cancer                                                                                                                                              | <a href="https://clinicaltrials.gov/show/NCT00673205">https://clinicaltrials.gov/show/NCT00673205</a>         | 2008 |         |        |         | Tipo de publicación equivocada |
| NCT03732820                                                                                                                                                                                                      | Study on Olaparib Plus Abiraterone as First-line Therapy in Men With Metastatic Castration-resistant Prostate Cancer                                                                                                   | <a href="https://clinicaltrials.gov/ct2/show/NCT03732820">https://clinicaltrials.gov/ct2/show/NCT03732820</a> | 2018 |         |        |         | Tipo de publicación equivocada |
| NCT05171816                                                                                                                                                                                                      | Study on Olaparib Plus Abiraterone as First-line Therapy in Men With Metastatic Castration-resistant Prostate Cancer (China Cohort)                                                                                    | <a href="https://clinicaltrials.gov/ct2/show/NCT05171816">https://clinicaltrials.gov/ct2/show/NCT05171816</a> | 2021 |         |        |         | Tipo de publicación equivocada |
| Chao, Z and Wang, Z and Li, L and Jiang, Y and Tang, Y and Wang, Y and Hao, X and Zhang, C and Guo, X and Yu, W and Cheng, F and Wang, Z                                                                         | Poly (ADP-ribose) Polymerase Inhibitors in Patients with Metastatic Castration-Resistant Prostate Cancer: A Meta-Analysis of Randomized Controlled Trials                                                              | Medicina (Kaunas, Lithuania)                                                                                  | 2023 | 59      | 12     |         | Comparación equivocada         |
| Fazekas, T and Széles, Á D and Teutsch, B and Csizmarik, A and Vékony, B and Váradi, A and Kói, T and Lang, Z and Ács, N and Kopa, Z and Hegyi, P and Hadaschik, B and Grünwald, V and Nyirády, P and Szarvas, T | Therapeutic sensitivity to standard treatments in BRCA positive metastatic castration-resistant prostate cancer patients—a systematic review and meta-analysis                                                         | Prostate Cancer and Prostatic Diseases                                                                        | 2023 | 26      | 4      | 665-672 | Artículo general               |
| NCT06060587                                                                                                                                                                                                      | Randomized Phase II Study of ADT + Abiraterone vs ADT + Docetaxel + Abiraterone                                                                                                                                        | <a href="https://clinicaltrials.gov/ct2/show/NCT06060587">https://clinicaltrials.gov/ct2/show/NCT06060587</a> | 2023 |         |        |         | Tipo de publicación equivocada |
| NCT04139772                                                                                                                                                                                                      | Docetaxel or Hormone Therapy as Second Line Treatment in Patients With Asymptomatic or Oligosymptomatic Metastatic Castration-resistant Prostate                                                                       | <a href="https://clinicaltrials.gov/show/NCT04139772">https://clinicaltrials.gov/show/NCT04139772</a>         | 2019 |         |        |         | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                                                                                                    | Título                                                                                                                                                                                                                                                        | Revista              | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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|                                                                                                                                                                                                                                                                                                                                                                                          | Cancer (mCRPC) Progressing After Abiraterone or Enzalutamide                                                                                                                                                                                                  |                      |      |         |        |         |                                |
| Jurincic, C D and Horlbeck, R and Klippel, K F                                                                                                                                                                                                                                                                                                                                           | Combined treatment (goserelin plus flutamide) versus monotherapy (goserelin alone) in advanced prostate cancer: a randomized study                                                                                                                            | Seminars in oncology | 1991 | 18      | 5      | 21-25   | No se encuentra texto completo |
| Sayyid, R K and Klaassen, Z and Berlin, A and Roy, S and Brandão, L R and Bernardino, R and Chavarriaga, J and Jiang, D M and Spratt, D E and Fleshner, N E and Wallis, C J D                                                                                                                                                                                                            | Poly(adenosine diphosphate-ribose) polymerase inhibitor combinations in first-line metastatic castrate-resistant prostate cancer setting: a systematic review and meta-analysis                                                                               | BJU International    | 2023 | 132     | 6      | 619-630 | Comparación equivocada         |
| AA, Azad and Bressel, M and Tan, H and Voskoboinik, M and Suder, A and AJ, Weickhardt and Guminski, A and RJ, Francis and Saghebi, J and Dhiantravan, N and AM, Joshua and Emmett, L and Horvath, L and DG, Murphy and Hsiao, E and Balakrishnar, B and Lin, P and Redfern, A and Macdonald, W and Ng, S and ST, Lee and DA, Pattison and Nadebaum, D and ID, Kirkwood and MS, Hofman    | Sequential [(177)Lu]Lu-PSMA-617 and docetaxel versus docetaxel in patients with metastatic hormone-sensitive prostate cancer (UpFrontPSMA): a multicentre, open-label, randomised, phase 2 study. PG - 1267-1276 LID - S1470-2045(24)00440-6 [pii] LID - 10.1 |                      |      |         | 1474   |         | Tipo de publicación equivocada |
| BM, Privé and MJR, Janssen and van Oort IM and CHJ, Muselaers and MA, Jonker and van Gemert WA and de Groot M and H, Westdorp and N, Mehra and JF, Verzijlbergen and TWJ, Scheenen and P, Zámecnik and JO, Barentsz and M, Gotthardt and W, Noordzij and WV, Vogel and AM, Bergman and van der Poel HG and AN, Vis and DE, Oprea-Lager and WR, Gerritsen and JA, Witjes and J, Nagarajah | Update to a randomized controlled trial of lutetium-177-PSMA in Oligo-metastatic hormone-sensitive prostate cancer: the BULLSEYE trial.                                                                                                                       | Trials               | 2021 | 22      | 1      | 768-768 | Tipo de publicación equivocada |

| Autor                                                                                                                                                            | Título                                                                                                                                                                                                                                                                                                   | Revista                                                                                                       | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Izumi, K and Mizokami, A and Takahara, S                                                                                                                         | 263MO Enzalutamide versus abiraterone plus prednisolone for Japanese non-metastatic castration-resistant prostate cancer patients: Sub-analysis from ENABLE for PCa, a multicenter, randomized controlled trial                                                                                          | Annals of Oncology                                                                                            | 2023 | 34      |        | S1575-S1576 | Tipo de publicación equivocada |
| NCT02058706                                                                                                                                                      | LHRH Analogue Therapy With Enzalutamide or Bicalutamide in Treating Patients With Hormone Sensitive Prostate Cancer                                                                                                                                                                                      | <a href="https://clinicaltrials.gov/show/NCT02058706">https://clinicaltrials.gov/show/NCT02058706</a>         | 2014 |         |        |             | Tipo de publicación equivocada |
| NCT02987543                                                                                                                                                      | Study of Olaparib (Lynparza™) Versus Enzalutamide or Abiraterone Acetate in Men With Metastatic Castration-Resistant Prostate Cancer (PROfound Study)                                                                                                                                                    | <a href="https://clinicaltrials.gov/show/NCT02987543">https://clinicaltrials.gov/show/NCT02987543</a>         | 2016 |         |        |             | Tipo de publicación equivocada |
| Hofman, M S and Emmett, L and Violet, J and A, Y Zhang and Lawrence, N J and Stockler, M and Francis, R J and Iravani, A and Williams, S and Azad, A and al., et | TheraP: a randomized phase 2 trial of 177 Lu-PSMA-617 theranostic treatment vs cabazitaxel in progressive metastatic castration-resistant prostate cancer (Clinical Trial Protocol ANZUP 1603)                                                                                                           | BJU international                                                                                             | 2019 | 124     |        | 5-13        | Tipo de publicación equivocada |
| NCT02200614                                                                                                                                                      | Efficacy and Safety Study of Darolutamide (ODM-201) in Men With High-risk Non-metastatic Castration-resistant Prostate Cancer                                                                                                                                                                            | <a href="https://clinicaltrials.gov/show/NCT02200614">https://clinicaltrials.gov/show/NCT02200614</a>         | 2014 |         |        |             | Tipo de publicación equivocada |
| Klotz, L and Boccon-Gibod, L and Shore, N D and Andreou, C and Persson, B E and Cantor, P and Jensen, J K and Olesen, T K and Schröder, F H                      | The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer                                                                                                                                                   | BJU international                                                                                             | 2008 | 102     | 11     | 1531-1538   | Población equivocada           |
| CF, Ng and CH, Yee and PK, Chiu and K, Wong and D, Lam and VW, Yuen and PT, Lai and JY, Teoh                                                                     | Patient Preference of Apalutamide Versus Enzalutamide for Recurrent or Metastatic Hormone-sensitive Prostate Cancer: An Open-label, Randomized, Crossover Trial.                                                                                                                                         | European urology oncology                                                                                     | 2024 | 7       | 6      | 1420-1430   | Desenlace equivocado           |
| NCT03764540                                                                                                                                                      | Docetaxel Versus Cabazitaxel Post Abiraterone or Enzalutamide                                                                                                                                                                                                                                            | <a href="https://clinicaltrials.gov/ct2/show/NCT03764540">https://clinicaltrials.gov/ct2/show/NCT03764540</a> | 2018 |         |        |             | Tipo de publicación equivocada |
| NCT04597125                                                                                                                                                      | Investigation of Radium-223 Dichloride (Xofigo), a Treatment That Gives Off Radiation That Helps Kill Cancer Cells, Compared to a Treatment That Inactivates Hormones (New Antihormonal Therapy, NAH) in Patients With Prostate Cancer That Has Spread to the Bone Getting Worse on or After Earlier NAH |                                                                                                               | 2020 |         |        |             | Tipo de publicación equivocada |



| Autor                                                                                                                                                                                                                                                                                                                                                                               | Título                                                                                                                                                                                                  | Revista                                                                                                       | Año  | Volumen | Número | Páginas    | Razón de exclusión              |
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| F, Saad and D, Cella and E, Basch and BA, Hadaschik and PN, Mainwaring and S, Oudard and JN, Graff and K, McQuarrie and S, Li and S, Hudgens and J, Lawson and A, Lopez-Gitlitz and MK, Yu and MR, Smith and EJ, Small                                                                                                                                                              | Effect of apalutamide on health-related quality of life in patients with non-metastatic castration-resistant prostate cancer: an analysis of the SPARTAN randomised, placebo-controlled, phase 3 trial. | The Lancet. Oncology                                                                                          | 2018 | 19      | 10     | 1404-1416  | Existe una versión más reciente |
| George, D J and Saad, F and Cookson, M S and Saltzstein, D R and Tutrone, R and Bossi, A and Brown, B and Selby, B and Lu, S and Buckley, D and al., et                                                                                                                                                                                                                             | Impact of Concomitant Prostate Cancer Medications on Efficacy and Safety of Relugolix Versus Leuprolide in Men With Advanced Prostate Cancer                                                            | Clinical genitourinary cancer                                                                                 | 2023 | 21      | 3      | 383-392.e2 | Comparación equivocada          |
| Z, Liu and T, Zhang and Z, Ma and S, Zheng and J, Chen and Z, Wu and X, Zheng and X, Li and Z, Liu                                                                                                                                                                                                                                                                                  | Systemic Management for Nonmetastatic Castration-resistant Prostate Cancer: A Systematic Review and Network Meta-Analysis.                                                                              | American journal of clinical oncology                                                                         | 2020 | 43      | 4      | 288-297    | Tratamiento equivocado          |
| P, Rajwa and B, Pradere and G, Gandaglia and van den Bergh RCN and I, Tsaur and SR, Shim and T, Yanagisawa and E, Laukhtina and K, Mori and H, Mostafaei and F, Quhal and P, Bryniarski and E, Compérat and G, Roubaud and C, Massard and AS, Merseburger and MS, Leapman and DE, Spratt and F, Saad and S, Joniau and AV, D'Amico and A, Briganti and SF, Shariat and G, Ploussard | Intensification of Systemic Therapy in Addition to Definitive Local Treatment in Nonmetastatic Unfavourable Prostate Cancer: A Systematic Review and Meta-analysis.                                     | European urology                                                                                              | 2022 | 82      | 1      | 82-96      | Tratamiento equivocado          |
| Gillessen, S and Procopio, G and Hayoz, S and Kremer, E and Schwitter, M and Caffo, O and Lorente, D and Pedrazzini, A and Roubaud, G and Nenan, S and al., et                                                                                                                                                                                                                      | Darolutamide Maintenance in Patients With Metastatic Castration-Resistant Prostate Cancer With Nonprogressive Disease After Taxane Treatment (SAKK 08/16)                                               | Journal of clinical oncology                                                                                  | 2023 | 41      | 20     | 3608-3615  | Artículo general                |
| NCT02799602                                                                                                                                                                                                                                                                                                                                                                         | Darolutamide in Addition to Standard Androgen Deprivation Therapy and Docetaxel in Metastatic Hormone-Sensitive Prostate Cancer                                                                         | <a href="https://clinicaltrials.gov/ct2/show/NCT02799602">https://clinicaltrials.gov/ct2/show/NCT02799602</a> | 2016 |         |        |            | Tipo de publicación equivocada  |

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| NCT06931340                                                                                                                                                                                                                 | Testing the Addition of Docetaxel (Chemotherapy) to the Usual Treatment (Hormonal Therapy and Apalutamide) for Metastatic Prostate Cancer, ASPIRE Trial                                                                                                       | <a href="https://clinicaltrials.gov/ct2/show/NCT06931340">https://clinicaltrials.gov/ct2/show/NCT06931340</a> | 2025 |         |        |           | Tipo de publicación equivocada |
| DR, Berthold and GR, Pond and F, Soban and de Wit R and M, Eisenberger and IF, Tannock                                                                                                                                      | Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer: updated survival in the TAX 327 study.                                                                                                                                | Journal of clinical oncology : official journal of the American Society of Clinical Oncology                  | 2008 | 26      | 2      | 242-245   | No se encuentra texto completo |
| Takayesu, J and Nasser, B and Xie, T and Suresh, K and Alumkal, J and Dess, R T and Reichert, Z and Schipper, M and Spratt, D E and Jackson, W C                                                                            | A Systematic Review and Network Meta-Analysis Assessing the Impact of Adding First Generation Non-Steroidal Anti-Androgens (NSAA) to LHRH Agonists (LHRHa) in Men Receiving Radiotherapy for Localized Prostate Cancer                                        | International Journal of Radiation Oncology Biology Physics                                                   | 2023 | 117     | 2      | e444-e445 | Tipo de publicación equivocada |
| NCT02685267                                                                                                                                                                                                                 | Docetaxel/Prednisone Versus Docetaxel/Prednisone and Enzalutamide in Castration-Resistant Prostate Cancer                                                                                                                                                     | <a href="https://clinicaltrials.gov/show/NCT02685267">https://clinicaltrials.gov/show/NCT02685267</a>         | 2016 |         |        |           | Tipo de publicación equivocada |
| Lunglmayr, G                                                                                                                                                                                                                | 'Zoladex' versus 'Zoladex' plus flutamide in the treatment of advanced prostate cancer. First interim analysis of an international trial. International Prostate Cancer Study Group                                                                           | Progress in clinical and biological research                                                                  | 1989 | 303     |        | 145-151   | No se encuentra texto completo |
| LC, Mendez and Dhar, A and Laidley, D and Moussa, M and JA, Gomez and Chin, J and TY, Lee and JD, Thiessen and Hoover, D and Surrey, K and Helou, J and Velker, V and RJ, Correa and D'Souza, D and Bayani, J and Bauman, G | The use of Lutetium-177 PSMA radioligand therapy with high dose rate brachytherapy for locally recurrent prostate cancer after previous definitive radiation therapy: a randomized, single-institution, phase I/II study (ROADSTER). PG - 362 LID - 10.1186/s |                                                                                                               |      |         | 1471   |           | Desenlace equivocado           |
|                                                                                                                                                                                                                             | Immediate versus deferred treatment for advanced prostatic cancer: initial results of the Medical Research Council Trial. The Medical Research Council Prostate Cancer Working Party Investigators Group. PG - 235-46                                         |                                                                                                               |      |         | 7      |           | Tipo de publicación equivocada |
| K, Mori and N, Miura and H, Mostafaei and F, Quhal and R, Sari Motlagh and B, Pradere and S, Kimura and T, Kimura and S, Egawa and A, Briganti                                                                              | Sequential therapy of abiraterone and enzalutamide in castration-resistant prostate cancer: a systematic review and meta-analysis.                                                                                                                            | Prostate cancer and prostatic diseases                                                                        | 2020 | 23      | 4      | 539-548   | Artículo general               |

| Autor                                                                                                                                                                                                | Título                                                                                                                                                                                                                                                                                                   | Revista                                                                                                                                                 | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| and PI, Karakiewicz and SF, Shariat                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                         |      |         |        |           |                                |
| G, Roviello and MR, Gatta Michelet and A, D'Angelo and S, Nobili and E, Mini                                                                                                                         | Role of novel hormonal therapies in the management of non-metastatic castration-resistant prostate cancer: a literature-based meta-analysis of randomized trials.                                                                                                                                        | Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico | 2020 | 22      | 7      | 1033-1039 | Diseño de estudio equivocado   |
| K, Fizazi and N, Shore and TL, Tammela and A, Ulys and E, Vjaters and S, Polyakov and M, Jievals and M, Luz and B, Alekseev and I, Kuss and C, Kappeler and A, Snapir and T, Sarapohja and MR, Smith | Darolutamide in Nonmetastatic, Castration-Resistant Prostate Cancer.                                                                                                                                                                                                                                     | The New England journal of medicine                                                                                                                     | 2019 | 380     | 13     | 1235-1246 | Comparación equivocada         |
|                                                                                                                                                                                                      | [Adjuvant Therapy in High-Risk Prostate Cancer after Radical Prostatectomy - A Randomized, open-label, Phase 2 Study of Adjuvant Apalutamide or Standard of Care in Subjects with High-risk, Localized or Locally Advanced Prostate Cancer After Radical Prostatectomy (ADAM) - Study AP 116/21 of AUO]. | Aktuelle Urologie                                                                                                                                       | 2023 | 54      | 1      | 21-23     | Tratamiento equivocado         |
| L, Wang and C, Paller and H, Hong and L, Rosman and A, De Felice and O, Brawley and GC, Alexander                                                                                                    | Comparison of Treatments for Nonmetastatic Castration-Resistant Prostate Cancer: Matching-Adjusted Indirect Comparison and Network Meta-Analysis.                                                                                                                                                        | Journal of the National Cancer Institute                                                                                                                | 2022 | 114     | 2      | 191-202   | No se encuentra texto completo |
| K, Patell and M, Kurian and JA, Garcia and P, Mendiratta and PC, Barata and AY, Jia and DE, Spratt and JR, Brown                                                                                     | Lutetium-177 PSMA for the treatment of metastatic castrate resistant prostate cancer: a systematic review.                                                                                                                                                                                               | Expert review of anticancer therapy                                                                                                                     | 2023 | 23      | 7      | 731-744   | Diseño de estudio equivocado   |
|                                                                                                                                                                                                      | Abiraterone. After prostate cancer treatment failure: 4-month survival advantage. PG - 147-9                                                                                                                                                                                                             |                                                                                                                                                         |      |         | 1167   |           | Tipo de publicación equivocada |
| X, Wang and H, Yang and X, Hu and W, Wang and X, Yu and S, Wang and X, Zhang and L, Liu                                                                                                              | Comparing the clinical efficacy and safety of abiraterone and enzalutamide in metastatic castration-resistant prostate cancer: A systematic review and meta-analysis.                                                                                                                                    | Journal of oncology pharmacy practice : official publication of the International Society of Oncology                                                   | 2021 | 27      | 3      | 614-622   | Diseño de estudio equivocado   |

| Autor                                                                                                                                                                                                                                                           | Título                                                                                                                                                                                                                                       | Revista                                                                         | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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|                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                              | Pharmacy Practitioners                                                          |      |         |        |           |                                |
| CN, Sternberg and de Bono JS<br>FAU - Chi, K N and Chi KN<br>FAU - Fizazi, K and Fizazi K<br>FAU - Mulders, P and Mulders P<br>FAU - Cerbone, L and Cerbone L<br>FAU - Hirmand, M and Hirmand M<br>FAU - Forer, D and Forer D<br>FAU - Scher, H I and HI, Scher | Improved outcomes in elderly patients with metastatic castration-resistant prostate cancer treated with the androgen receptor inhibitor enzalutamide: results from the phase III AFFIRM trial. PG - 429-34 LID - 10.1093/annonc/mdt571 [doi] |                                                                                 |      |         | 1569   |           | Tipo de publicación equivocada |
| CH, Chen and YS, Pu                                                                                                                                                                                                                                             | Adjuvant androgen-deprivation therapy following prostate total cryoablation in high-risk localized prostate cancer patients - Open-labeled randomized clinical trial.                                                                        | Cryobiology                                                                     | 2018 | 82      |        | 88-92     | Tratamiento equivocado         |
| S, Feyerabend and F, Saad and NJ, Perualila and S, Van Sanden and J, Diels and T, Ito and P, De Porre and K, Fizazi                                                                                                                                             | Adjusting Overall Survival Estimates for Treatment Switching in Metastatic, Castration-Sensitive Prostate Cancer: Results from the LATITUDE Study.                                                                                           | Targeted oncology                                                               | 2019 | 14      | 6      | 681-688   | Población equivocada           |
| von Eyben FE and G, Roviello and T, Kiljunen and C, Uprimny and I, Virgolini and K, Kairemo and T, Joensuu                                                                                                                                                      | Third-line treatment and (177)Lu-PSMA radioligand therapy of metastatic castration-resistant prostate cancer: a systematic review.                                                                                                           | European journal of nuclear medicine and molecular imaging                      | 2018 | 45      | 3      | 496-508   | Población equivocada           |
| KK, Ternov and AB, Nolsøe and O, Bratt and M, Fode and H, Lindberg and C, Kistorp and G, Palapattu and TW, Klausen and J, Sønksen and PB, Østergren                                                                                                             | Quality of life in men with metastatic castration-resistant prostate cancer treated with enzalutamide or abiraterone: a systematic review and meta-analysis.                                                                                 | Prostate cancer and prostatic diseases                                          | 2021 | 24      | 4      | 948-961   | Comparación equivocada         |
| S, Satapathy and RK, Sahoo and C, Bal                                                                                                                                                                                                                           | [(177)Lu]Lu-PSMA-Radioligand Therapy Efficacy Outcomes in Taxane-Naïve Versus Taxane-Treated Patients with Metastatic Castration-Resistant Prostate Cancer: A Systematic Review and Metaanalysis.                                            | Journal of nuclear medicine : official publication, Society of Nuclear Medicine | 2023 | 64      | 8      | 1266-1271 | Comparación equivocada         |
| A, Josefsson and Å, Jellvert and E, Holmberg and K, Brasso and P, Meidahl Petersen and S, Aaltomaa and M, Luukka and P, Verhagen and de Wit R and G, Ahlgren and O, Andrén and E,                                                                               | Effect of docetaxel added to bicalutamide in Hormone-Naïve non-metastatic prostate cancer with rising PSA, a randomized clinical trial (SPCG-14).                                                                                            | Acta oncologica (Stockholm, Sweden)                                             | 2023 | 62      | 4      | 372-380   | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                                                                         | Título                                                                                                                                                                                                                                                         | Revista                                                                                               | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Castellanos and M, Seke and A, Widmark and JE, Damber C, Kesch and BA, Hadaschik                                                                                                                                                                                              | Re: Active Surveillance Plus Enzalutamide Monotherapy vs Active Surveillance Alone in Patients with Low-risk or Intermediate-risk Localized Prostate Cancer: The ENACT Randomized Clinical Trial.                                                              | European urology                                                                                      | 2022 | 82      | 5      | 572-572     | Tipo de publicación equivocada |
| DR, Siemens and L, Klotz and A, Heidenreich and S, Chowdhury and A, Villers and B, Baron and van Os S and N, Hasabou and F, Wang and P, Lin and ND, Shore                                                                                                                     | Efficacy and Safety of Enzalutamide vs Bicalutamide in Younger and Older Patients with Metastatic Castration Resistant Prostate Cancer in the TERRAIN Trial.                                                                                                   | The Journal of urology                                                                                | 2018 | 199     | 1      | 147-154     | Comparación equivocada         |
| N, Matsubara and K, Nishimura and S, Kawakami and JY, Joung and H, Uemura and T, Goto and TG, Kwon and M, Sugimoto and M, Kato and SS, Wang and ST, Pang and CH, Chen and T, Fujita and M, Nii and L, Shen and M, Dujka and M, Hussain and de Bono J                          | Olaparib in patients with mCRPC with homologous recombination repair gene alterations: PROfound Asian subset analysis.                                                                                                                                         | Japanese journal of clinical oncology                                                                 | 2022 | 52      | 5      | 441-448     | Población equivocada           |
| AP, Fay and Fizazi, K and Matsubara, N and AA, Azad and Saad, F and U, De Giorgi and JY, Joung and PCC, Fong and RJ, Jones and Zschäbitz, S and Oldenburg, J and ND, Shore and Dunshee, C and Carles, J and Cislo, P and Chang, J and CG, Healy and Niyazov, A and Agarwal, N | First-line talazoparib plus enzalutamide versus placebo plus enzalutamide in men with metastatic castration-resistant prostate cancer and homologous recombination repair gene alterations: patient-reported outcomes from the randomised, double-blind, place |                                                                                                       |      |         | 1474   |             | Tipo de publicación equivocada |
| X, Xiong and S, Qiu and X, Yi and H, Xu and H, Lei and D, Liao and S, Bai and G, Peng and Q, Wei and J, Ai and L, Yang                                                                                                                                                        | Efficacy and safety of bipolar androgen therapy in mCRPC after progression on abiraterone or enzalutamide: A systematic review.                                                                                                                                | Urologic oncology                                                                                     | 2022 | 40      | 1      | 4.e19-4.e28 | Comparación equivocada         |
| NCT02346578                                                                                                                                                                                                                                                                   | Comparative Study of Alternative Antiandrogen (AA) Therapy and Early Initiating of Enzalutamide for Castration-                                                                                                                                                | <a href="https://clinicaltrials.gov/show/NCT02346578">https://clinicaltrials.gov/show/NCT02346578</a> | 2015 |         |        |             | Población equivocada           |

| Autor                                                                                                                                             | Título                                                                                                                                                                                                                                                          | Revista                                                                                                       | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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|                                                                                                                                                   | resistant Prostate Cancer (CRPC) After Combined Androgen Blockade (CAB) Therapy                                                                                                                                                                                 |                                                                                                               |      |         |        |           |                                |
| Haefliger, J M                                                                                                                                    | Randomized study comparing zoladex versus zoladex plus flutamide in treatment of advanced cancer of the prostate                                                                                                                                                | Helvetica chirurgica acta                                                                                     | 1992 | 59      | 3      | 477-483   | No se encuentra texto completo |
| NCT00295750                                                                                                                                       | The Efficacy and Safety of Degarelix One Month Dosing Regimens in Prostate Cancer                                                                                                                                                                               | <a href="https://clinicaltrials.gov/show/NCT00295750">https://clinicaltrials.gov/show/NCT00295750</a>         | 2006 |         |        |           | Tipo de publicación equivocada |
| NCT02034552                                                                                                                                       | A Randomized Phase IIa Efficacy and Safety Study of Radium-223 Dichloride With Abiraterone Acetate or Enzalutamide in Metastatic Castration-resistant Prostate Cancer (CRPC)                                                                                    | <a href="https://clinicaltrials.gov/show/NCT02034552">https://clinicaltrials.gov/show/NCT02034552</a>         | 2013 |         |        |           | Tipo de publicación equivocada |
| NCT04663997                                                                                                                                       | 177 LuPSMA-617 vs Docetaxel in Metastatic Castration Resistant and PSMA-Positive Prostate Cancer                                                                                                                                                                | <a href="https://clinicaltrials.gov/ct2/show/NCT04663997">https://clinicaltrials.gov/ct2/show/NCT04663997</a> | 2020 |         |        |           | Tipo de publicación equivocada |
| Zhou, F and Gongqian, Z and Guo, H and Hu, Z and Zhang, X and He, D and He, Z and Zhang, D and Li, Y and Kadeerbai, H and Liu, Y and Ye, D        | 1795P China ARCHES: A multicenter phase III randomized double-blind placebo (PBO)-controlled efficacy and safety trial of enzalutamide (ENZA) + androgen deprivation therapy (ADT) vs PBO + ADT in Chinese patients (pts) with metastatic hormone-sensitive pro | Annals of Oncology                                                                                            | 2023 | 34      |        | S971-S971 | Tipo de publicación equivocada |
| Slovin, S F and Knudsen, K and Halabi, S and de Leeuw, R and Shafi, A and Kang, P and Wolf, S and Luo, B and Gopalan, A and Curley, T and al., et | Randomized Phase II Multicenter Trial of Abiraterone Acetate With or Without Cabazitaxel in the Treatment of Metastatic Castration-Resistant Prostate Cancer                                                                                                    | Journal of clinical oncology                                                                                  | 2023 | 41      | 32     | 5015-5024 | Comparación equivocada         |
| NCT00974311                                                                                                                                       | Safety and Efficacy Study of MDV3100 in Patients With Castration-Resistant Prostate Cancer Who Have Been Previously Treated With Docetaxel-based Chemotherapy                                                                                                   | <a href="https://clinicaltrials.gov/show/NCT00974311">https://clinicaltrials.gov/show/NCT00974311</a>         | 2009 |         |        |           | Tipo de publicación equivocada |
| McLeod, D G and Iversen, P and See, W A and Morris, T and Armstrong, J and Wirth, M P                                                             | Bicalutamide 150 mg plus standard care vs standard care alone for early prostate cancer                                                                                                                                                                         | BJU International                                                                                             | 2006 | 97      | 2      | 247-254   | Población equivocada           |
| Dijkman, G A and Debruyne, F M and del Moral, P and Plasman, J W and Hoefakker,                                                                   | A randomised trial comparing the safety and efficacy of the Zoladex 10.8-mg depot, administered every 12 weeks, to that of the Zoladex 3.6-mg depot, administered every 4                                                                                       |                                                                                                               | 1995 | 27      | 1      | 43-46     | Población equivocada           |

| Autor                                                                                                                                                                                                                           | Título                                                                                                                                                                                                | Revista                                                                                                       | Año  | Volumen | Número | Páginas       | Razón de exclusión             |
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| J W and Idema, J G and Sykes, M                                                                                                                                                                                                 | weeks, in patients with advanced prostate cancer. The Dutch South East Cooperative Urological Group                                                                                                   |                                                                                                               |      |         |        |               |                                |
| Stenzl, A and Krivoshik, A and Baron, B and Hirmand, M and Armstrong, A                                                                                                                                                         | Efficacy and safety of enzalutamide plus androgen deprivation therapy vs placebo plus androgen deprivation therapy in men with metastatic hormone-sensitive prostate cancer: the ongoing ARCHES trial | Annals of oncology                                                                                            | 2016 | 27      |        | vi262-vi262   | Tipo de publicación equivocada |
| Turkes, A O and Peeling, W B and Griffiths, K                                                                                                                                                                                   | Treatment of patients with advanced cancer of the prostate: phase III trial, zoladex against castration; a study of the British Prostate Group                                                        | Journal of steroid biochemistry                                                                               | 1987 | 27      | 1      | 543-549       | Tipo de publicación equivocada |
| Yanagisawa, T and Rajwa, P and Kawada, T and Mori, K and Fukuokaya, W and Petrov, P and Quhal, F and Laukhtina, E and Von Deimling, M and Bianchi, A and Majdoub, M and Pradere, B and Kramer, G and Kimura, T and Shariat, S F | Efficacy of Systemic Treatment in Prostate Cancer Patients with Visceral Metastasis: A Systematic Review, Meta-analysis, and Network Meta-analysis                                                    | Journal of Urology                                                                                            | 2023 | 210     | 3      | 416-428       | No se encuentra texto completo |
| NCT02543255                                                                                                                                                                                                                     | Anti-Androgens and Cabazitaxel in Defining Complete Response in Prostatectomy (ACDC Trial)                                                                                                            | <a href="https://clinicaltrials.gov/ct2/show/NCT02543255">https://clinicaltrials.gov/ct2/show/NCT02543255</a> | 2015 |         |        |               | Tipo de publicación equivocada |
| NCT03012321                                                                                                                                                                                                                     | Abiraterone/Prednisone, Olaparib, or Abiraterone/Prednisone + Olaparib in Patients With Metastatic Castration-Resistant Prostate Cancer With DNA Repair Defects                                       | <a href="https://clinicaltrials.gov/show/NCT03012321">https://clinicaltrials.gov/show/NCT03012321</a>         | 2017 |         |        |               | Tipo de publicación equivocada |
| Sandhu, S K and Violet, J A and Ferdinandus, J and Thang, S-P and Iravani, A and Guo, C and Kong, G and Kumar, A R and Akhurst, T J and Beaulieu, A and al., et                                                                 | Lutetium-177 PSMA617 theranostics in metastatic castrate-resistant prostate cancer (mCRPC): interim results of a phase II trial                                                                       | Journal of clinical oncology                                                                                  | 2018 | 36      | 15     |               | Tipo de publicación equivocada |
| NCT03392428                                                                                                                                                                                                                     | A Trial of 177Lu-PSMA617 Theranostic Versus Cabazitaxel in Progressive Metastatic Castration Resistant Prostate Cancer                                                                                | <a href="https://clinicaltrials.gov/show/NCT03392428">https://clinicaltrials.gov/show/NCT03392428</a>         | 2017 |         |        |               | Tipo de publicación equivocada |
| SE, Petersen and M, Høyer                                                                                                                                                                                                       | Androgen Deprivation Therapy Combined With Particle Therapy for Prostate Cancer: A Systematic Review.                                                                                                 | Frontiers in oncology                                                                                         | 2021 | 11      |        | 695647-695647 | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                                                                                                                                                | Título                                                                                                                                                                                                                                                        | Revista                                                                                               | Año  | Volumen | Número | Páginas           | Razón de exclusión             |
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| Berkut, M V and Artemjeva, A S and Reva, S A and Tolmachev, S S and Petrov, S B and Nosov, A K                                                                                                                                                                                                                                                       | Oncological results of neoadjuvant chemohormonal therapy in patients with high and very high-risk prostate cancer                                                                                                                                             | Onkourologiya                                                                                         | 2020 | 16      | 1      | 54-63             | Tratamiento equivocado         |
| NCT01949337                                                                                                                                                                                                                                                                                                                                          | Enzalutamide With or Without Abiraterone and Prednisone in Treating Patients With Castration-Resistant Metastatic Prostate Cancer                                                                                                                             | <a href="https://clinicaltrials.gov/show/NCT01949337">https://clinicaltrials.gov/show/NCT01949337</a> | 2013 |         |        |                   | Tipo de publicación equivocada |
| Smith, M and Parker, C and Saad, F and Miller, K and Tombal, B and QS, Ng and Boegemann, M and Matveev, V and JM, Piulats and LE, Zucca and Karyakin, O and Kimura, G and Matsubara, N and WC, Nahas and Nolè, F and Rosenbaum, E and Heidenreich, A and Kakehi, Y and Zhang, A and Krissel, H and Teufel, M and Shen, J and Wagner, V and Higano, C | Addition of radium-223 to abiraterone acetate and prednisone or prednisolone in patients with castration-resistant prostate cancer and bone metastases (ERA 223): a randomised, double-blind, placebo-controlled, phase 3 trial. PG - 408-419 LID - S1470-204 |                                                                                                       |      |         | 1474   |                   | Tipo de publicación equivocada |
| Wallis, C J D and Klaassen, Z and Jackson, W C and Dess, R T and Reichert, Z R and Sun, Y and Spratt, D E                                                                                                                                                                                                                                            | Olaparib vs Cabazitaxel in Metastatic Castration-Resistant Prostate Cancer                                                                                                                                                                                    | JAMA network open                                                                                     | 2021 | 4       | 5      | e2110950-e2110950 | Comparación equivocada         |
| NCT02379390                                                                                                                                                                                                                                                                                                                                          | Cabazitaxel Versus the Switch to Alternative AR Targeted Therapy Enzalutamide or Abiraterone in Metastatic Castration-Resistant Prostate Cancer (mCRPC) Primary Resistant Patients to Abiraterone or Enzalutamide                                             | <a href="https://clinicaltrials.gov/show/NCT02379390">https://clinicaltrials.gov/show/NCT02379390</a> | 2015 |         |        |                   | Tipo de publicación equivocada |
| Gu, C and Wang, Z and Lin, T and Liu, Z and Han, W and Zhang, X and Liang, C and Liu, H and Yu, Y and Xu, Z and Liu, S and Wang, J and Jia, L and Yao, X and Liao, W and Fu, C and Tan, Z and He, G and Zhu, G and Fan, R and Yang, W and Chen, X and Liu, Z and Zhong, L and Shi, B and Ding, D and Chen, S and Wei,                                | Efficacy and safety of LY01005 versus goserelin implant in Chinese patients with prostate cancer: A multicenter, randomized, open-label, phase III, non-inferiority trial                                                                                     | Chinese Medical Journal                                                                               | 2023 | 136     | 10     | 1207-1215         | Tipo de publicación equivocada |



| Autor                                                                                                                                                                                                                                                                                                                                                                                          | Título                                                                                                                                                                                                                                                      | Revista                                                                                                       | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| J and Yao, X and Chen, M and Lu, Z and Xie, Q and Hu, Z and Wang, Y and Guo, H and Fan, T and Liang, Z and Chen, P and Wang, W and Xu, T and Li, C and Xing, J and Liao, H and He, D and Wu, Z and Yu, J and Feng, Z and Yang, M and Dou, Q and Zeng, Q and Li, Y and Gou, X and Zhou, G and Wang, X and Zhu, R and Zhang, Z and Zhang, B and Tan, W and Qu, X and Sun, H and Gan, T and Ye, D |                                                                                                                                                                                                                                                             |                                                                                                               |      |         |        |         |                                |
| Riaz, I B and Naqvi, S A A and He, H and Asghar, N and Siddiqi, R and Liu, H and Singh, P and Childs, D S and Ravi, P and Hussain, S A and Murad, M H and Boorjian, S A and Sweeney, C and Van Allen, E M and Bryce, A H                                                                                                                                                                       | First-line Systemic Treatment Options for Metastatic Castration-Sensitive Prostate Cancer: A Living Systematic Review and Network Meta-analysis                                                                                                             | JAMA Oncology                                                                                                 | 2023 | 9       | 5      | 635-645 | Comparación equivocada         |
| NCT02257736                                                                                                                                                                                                                                                                                                                                                                                    | An Efficacy and Safety Study of Apalutamide (JNJ-56021927) in Combination With Abiraterone Acetate and Prednisone Versus Abiraterone Acetate and Prednisone in Participants With Chemotherapy-naïve Metastatic Castration-resistant Prostate Cancer (mCRPC) | <a href="https://clinicaltrials.gov/ct2/show/NCT02257736">https://clinicaltrials.gov/ct2/show/NCT02257736</a> | 2014 |         |        |         | Tipo de publicación equivocada |
| Yanagisawa, T and Kawada, T and Rajwa, P and Mostafaei, H and Motlagh, R S and Qahal, F and Laukhtina, E and König, F and Pallauf, M and Pradere, B and Karakiewicz, P I and Nyirady, P and Kimura, T and Egawa, S and Shariat, S F                                                                                                                                                            | Sequencing impact and prognostic factors in metastatic castration-resistant prostate cancer patients treated with cabazitaxel: A systematic review and meta-analysis                                                                                        | Urologic Oncology: Seminars and Original Investigations                                                       | 2023 | 41      | 4      | 177-191 | Desenlace equivocado           |
| Denis, L J and Keuppens, F and Smith, P H and Whelan, P and de Moura, J L and Newling, D and Bono, A and Sylvester, R                                                                                                                                                                                                                                                                          | Maximal androgen blockade: final analysis of EORTC phase III trial 30853. EORTC Genito-Urinary Tract Cancer Cooperative Group and the EORTC Data Center                                                                                                     | European urology                                                                                              | 1998 | 33      | 2      | 144-151 | Artículo general               |

| Autor                                                                                                                                                                                                                        | Título                                                                                                                                                                                                                                                        | Revista                                                                            | Año  | Volumen | Número | Páginas           | Razón de exclusión             |
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| Vaishampayan, U N and Heilbrun, L K and Monk, P and Tejwani, S and Sonpavde, G and Smith, D and Jasti, P and Dobson, K and Heath, E I and Cher, M L and al., et                                                              | Randomized trial of enzalutamide versus bicalutamide in combination with androgen deprivation in metastatic hormone sensitive prostate cancer: a Prostate Cancer Clinical Trials Consortium trial                                                             | Journal of clinical oncology                                                       | 2018 | 36      | 6      |                   | Tipo de publicación equivocada |
| Zhang, X and Zhang, G and Wang, J and Wang, Y                                                                                                                                                                                | Luteinizing hormone-releasing hormone agonists versus orchiectomy in the treatment of prostate cancer: A systematic review                                                                                                                                    | Frontiers in Endocrinology                                                         | 2023 | 14      |        |                   | Población equivocada           |
| Usmani, N and Ghosh, S and KP, Sanghera and AD, Ong and Koul, R and Dubey, A and Ahmed, S and Quon, H and Yee, D and Parliament, M and Sivananthan, G and Hunter, W and Danielson, B and Rowe, L and McDonald, M and JO, Kim | Metformin for Prevention of Anthropometric and Metabolic Complications of Androgen Deprivation Therapy in Prostate Cancer Patients Receiving Radical Radiotherapy: A Phase II Randomized Controlled Trial. PG - 317-326 LID - S0360-3016(22)00747-7 [pii] LID |                                                                                    |      |         | 1879   |                   | Tipo de publicación equivocada |
| O'Sullivan, N and Temperley, H C and Davey, M G and Naughton, A P and Casey, R G                                                                                                                                             | Surgical versus medical castration in the treatment of metastatic prostate cancer; A systematic review and meta-analysis                                                                                                                                      | European Urology                                                                   | 2023 | 83      |        | S1431-S1431       | Tratamiento equivocado         |
| Chi, K N and Taavitsainen, S and Iqbal, N and Ferrario, C and Ong, M and Wadhwa, D and Hotte, S J and Lo, G and Tran, B and Azad, A and al., et                                                                              | A randomized phase II study of cabazitaxel (CAB) vs (ABI) abiraterone or (ENZ) enzalutamide in poor prognosis metastatic castrationresistant prostate cancer (mCRPC)                                                                                          | Annals of oncology                                                                 | 2018 | 29      |        | viii271-viii272   | Tipo de publicación equivocada |
| Nilsson, S and Cislo, P and Sartor, O and Vogelzang, N J and Coleman, R E and O'Sullivan, J M and Reuning-Scherer, J and Shan, M and Zhan, L and Parker, C                                                                   | Patient-reported quality-of-life analysis of radium-223 dichloride from the phase III ALSYMPCA study                                                                                                                                                          | Annals of oncology : official journal of the european society for medical oncology | 2016 | 27      | 5      | 868-874           | Comparación equivocada         |
| Vaishampayan, U N and Heilbrun, L and Monk, P and Sonpavde, G and Tejwani, S and Heath, E I and Fontana, J and Chinni, S                                                                                                     | Randomized trial of androgen deprivation therapy (ADT) + enzalutamide (Arm A) versus ADT + bicalutamide (Arm B) in metastatic hormone sensitive prostate cancer (mHSPC)                                                                                       | Annals of oncology : official journal of the european society for medical oncology | 2018 | 29      |        | viii276--viii276- | Tipo de publicación equivocada |
| Jocham, D                                                                                                                                                                                                                    | Leuporelin three-month depot in the treatment of advanced and metastatic prostate cancer: long-term follow-up results. PG - 18-24; discussion 35                                                                                                              |                                                                                    |      |         | 42     |                   | Tipo de publicación equivocada |

| Autor                                                                                                                                                                          | Título                                                                                                                                                                                                                                    | Revista                             | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Iguchi, T and Kimura, G and Fukasawa, S and Suzuki, H and Uemura, H and Nishimura, K and Matsumoto, H and Yokomizo, A and Armstrong, A J and Rosbrook, B and al., et           | Enzalutamide with androgen deprivation therapy in Japanese men with metastatic hormone-sensitive prostate cancer: a subgroup analysis of the phase III ARCHES study                                                                       | International journal of urology    | 2021 | 28      | 7      | 765-773   | Tipo de publicación equivocada |
| Souhami, L and Bae K FAU - Pilepich, Miljenko and Pilepich M FAU - Sandler, Howard and Sandler, H                                                                              | Timing of salvage hormonal therapy in prostate cancer patients with unfavorable prognosis treated with radiotherapy: a secondary analysis of Radiation Therapy Oncology Group 85-31. PG - 1301-6 LID - 10.1016/j.ijrobp.2009.10.007 [doi] |                                     |      |         | 1879   |           | Tipo de publicación equivocada |
| Akaza, H and Isaka S FAU - Usami, M and Usami M FAU - Kanetake, H and Kanetake H FAU - Kotake, T and Kotake T FAU - Koiso, K and Koiso K FAU - Aso, Y and Aso, Y               | Recommended dose of flutamide with LH-RH agonist therapy in patients with advanced prostate cancer. PG - 468-71                                                                                                                           |                                     |      |         | 919    |           | Tipo de publicación equivocada |
| Merseburger, A S and Attard, G and Astrom, L and Matveev, V B and Bracarda, S and Esen, A and Feyerabend, S and Senkus, E and Lopez-Brea Piqueras, M and Boysen, G and al., et | Continuous enzalutamide after progression of metastatic castration-resistant prostate cancer treated with docetaxel (PRESIDE): an international, randomised, phase 3b study                                                               | The lancet. Oncology                | 2022 | 23      | 11     | 1398-1408 | Comparación equivocada         |
| Chen, J and Yuan, Y and Fang, M and Zhu, Y and Sun, X and Lou, Y and Xin, Y and Zhou, F                                                                                        | Androgen deprivation therapy and radiotherapy in intermediate-risk prostate cancer: A systematic review and meta-analysis                                                                                                                 | Frontiers in Endocrinology          | 2023 | 13      |        |           | Comparación equivocada         |
| Gratzke, C and Niu, C and Poehlein, C and Burgents, J                                                                                                                          | Keynote-991: phase 3 study of pembrolizumab plus enzalutamide and androgen deprivation therapy (ADT) for patients with metastatic hormone-sensitive prostate cancer (MHSPP)                                                               | Journal for immunotherapy of cancer | 2020 | 8       |        | A211-A211 | Tipo de publicación equivocada |
| Schulze, H and Kaldenhoff H FAU - Senge, T and Senge, T                                                                                                                        | Evaluation of total versus partial androgen blockade in the treatment of advanced prostatic cancer. PG - 193-7                                                                                                                            |                                     |      |         | 42     |           | Tipo de publicación equivocada |
| Merseburger, A S and Suttman, H                                                                                                                                                | TITAN study: evaluation of apalutamide in patients with metastatic hormone-sensitive prostate cancer - Treatment of metastatic hormone-sensitive prostate cancer (mHSPP)                                                                  | Aktuelle Urologie                   | 2021 | 52      | 2      | 155-160   | Comparación equivocada         |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Título                                                                                                                                                                               | Revista                                                                                               | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Darolutamide Slows Metastasis in Prostate Cancer                                                                                                                                     | Cancer discovery                                                                                      | 2019 | 9       | 4      | OF6-OF6 | Tipo de publicación equivocada |
| A, Pereira-Salgado and EM, Kwan and B, Tran and P, Gibbs and J, De Bono and M, IJzerman                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Systematic Review of Efficacy and Health Economic Implications of Real-world Treatment Sequencing in Prostate Cancer: Where Do the Newer Agents Enzalutamide and Abiraterone Fit in? | European urology focus                                                                                | 2021 | 7       | 4      | 752-763 | Tratamiento equivocado         |
| Teply, B A and Antonarakis, E S and Carducci, M A and Paller, C J and Wang, H and Cao, H and Spitz, A N and Luo, J and Eisenberger, M A and Denmeade, S R                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | A randomized phase II study comparing bipolar androgen therapy vs. Enzalutamide in asymptomatic men with castration resistant metastatic prostate cancer: the TRANSFORMER trial      | Journal of clinical oncology                                                                          | 2015 | 33      | 15     |         | Tipo de publicación equivocada |
| NCT01946165                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Abiraterone Acetate Plus LHRH Agonist and Enzalutamide                                                                                                                               | <a href="https://clinicaltrials.gov/show/NCT01946165">https://clinicaltrials.gov/show/NCT01946165</a> | 2013 |         |        |         | Tipo de publicación equivocada |
| ND, James and de Bono JS and MR, Spears and NW, Clarke and MD, Mason and DP, Dearnaley and AWS, Ritchie and CL, Amos and C, Gilson and RJ, Jones and D, Matheson and R, Millman and G, Attard and S, Chowdhury and WR, Cross and S, Gillesen and CC, Parker and JM, Russell and DR, Berthold and C, Brawley and F, Adab and S, Aung and AJ, Birtle and J, Bowen and S, Brock and P, Chakraborti and C, Ferguson and J, Gale and E, Gray and M, Hingorani and PJ, Hoskin and JF, Lester and ZI, Malik and F, McKinna and N, McPhail and J, Money-Kyrle and J, O'Sullivan and O, Parikh and A, Protheroe and A, Robinson and NN, Srihari and C, Thomas and J, Wagstaff and J, | Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy.                                                                                                         | The New England journal of medicine                                                                   | 2017 | 377     | 4      | 338-351 | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                                                                                                 | Título                                                                                                                                                                     | Revista                                                                                      | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Wylie and A, Zarkar and MKB, Parmar and MR, Sydes                                                                                                                                                                                                                                                     |                                                                                                                                                                            |                                                                                              |      |         |        |           |                                |
| Riaz, I B and Naqvi, S A A and He, H and Siddiqi, R and Asghar, N and Ravi, P and Hussain, S A and Singh, P and Bryce, A H                                                                                                                                                                            | A living interactive systematic review and network meta-analysis evaluating systemic therapies in metastatic castration-sensitive prostate cancer (mCSPC)                  | Journal of Clinical Oncology                                                                 | 2023 | 41      | 6      | 193-193   | Tipo de publicación equivocada |
| Naqvi, S A A and Riaz, I B and Imran, M and Zafar, M D B and Faisal, K S and Riaz, Z B and Singh, P and Bryce, A H                                                                                                                                                                                    | Deep prostate-specific antigen response and overall survival in patients with metastatic castration-sensitive prostate cancer: A systematic review and meta-analysis       | Journal of Clinical Oncology                                                                 | 2023 | 41      | 6      | 195-195   | Tipo de publicación equivocada |
| F, Saad and E, Vjaters and N, Shore and D, Olmos and N, Xing and de Santana Gomes AJ, Pereira and de Andrade Mota A, Cesar and P, Salman and M, Jievaltas and A, Ulys and M, Jakubovskis and E, Kopyltsov and W, Han and L, Nevalaita and I, Testa and MA, Le Berre and I, Kuss and KP, Haresh        | Darolutamide in Combination With Androgen-Deprivation Therapy in Patients With Metastatic Hormone-Sensitive Prostate Cancer From the Phase III ARANOTE Trial.              | Journal of clinical oncology : official journal of the American Society of Clinical Oncology | 2024 | 42      | 36     | 4271-4281 | Tratamiento equivocado         |
| J, Carles and E, Gallardo and M, Doménech and A, Font and J, Bellmunt and M, Figols and B, Mellado and MI, Sáez and C, Suárez and MJ, Méndez and P, Maroto and R, Luque and de Portugal T and R, Aldabo and T, Bonfill and R, Morales-Barrera and J, García and S, Maciá and X, Maldonado and P, Foro | Phase 2 Randomized Study of Radiation Therapy and 3-Year Androgen Deprivation With or Without Concurrent Weekly Docetaxel in High-Risk Localized Prostate Cancer Patients. | International journal of radiation oncology, biology, physics                                | 2019 | 103     | 2      | 344-352   | Tratamiento equivocado         |
| Chung, B H and Huang, J and Uemura, H and Choi, Y D and Ye, Z Q and Suzuki, H and Kang, T W and He, D L and Joung, J Y and Brookman-May, S D and al., et                                                                                                                                              | Apalutamide for metastatic castration-sensitive prostate cancer: final analysis of the Asian subpopulation in the TITAN trial                                              | Asian journal of andrology                                                                   | 2023 | 25      | 6      | 653-661   | Tipo de publicación equivocada |
| Hussain, M and Tangen, C M and Thompson, I M and Swanson, G P and Peter                                                                                                                                                                                                                               | Adjuvant androgen deprivation (AD) +/- mitoxantrone + prednisone (MP) in patients with high-risk prostate cancer (PC) post                                                 | Journal of clinical oncology                                                                 | 2017 | 35      | 15     |           | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                          | Título                                                                                                                                                                | Revista                                                                                                                      | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Wood, D and Sakr, W and Ann Dawson, N and Haas, N B and Flaig, T W and Dorff, T B and al., et                                                                                                                                  | radical prostatectomy (RP): phase III intergroup trial S9921                                                                                                          |                                                                                                                              |      |         |        |           |                                |
| Morote, J and Vallejo C FAU - Lorente, J A and Lorente JA FAU - Encabo, G and Encabo G FAU - López Pacios, M A and López Pacios MA FAU - de Torres, J A and de Torres JA FAU - Soler Roselló, A and A, Soler Roselló           | [Final results of complete hormone blockade versus monotherapy in prostatic metastatic cancer. PSA implications]. PG - 604-10                                         |                                                                                                                              |      |         | 210    |           | No se encuentra texto completo |
| M, Wenzel and C, Würnschimmel and L, Nocera and C, Collà Ruvolo and Z, Tian and SF, Shariat and F, Saad and A, Briganti and D, Tilki and M, Graefen and LA, Kluth and FC, Roos and P, Mandel and FKH, Chun and PI, Karakiewicz | Overall Survival After Systemic Treatment in High-volume Versus Low-volume Metastatic Hormone-sensitive Prostate Cancer: Systematic Review and Network Meta-analysis. | European urology focus                                                                                                       | 2022 | 8       | 2      | 399-408   | Tratamiento equivocado         |
| Rizzo, M and Mazzei T FAU - Mini, E and Mini E FAU - Bartoletti, R and Bartoletti R FAU - Periti, P and Periti, P                                                                                                              | Leuprorelin acetate depot in advanced prostatic cancer: a phase II multicentre trial. PG - 114-25                                                                     |                                                                                                                              |      |         | 300    |           | Tipo de publicación equivocada |
| O'Sullivan, N J and Temperley, H and Naughton, A and Casey, R G                                                                                                                                                                | Surgical Versus Medical Castration for Metastatic Prostate Cancer; A Systematic Review And Meta-Analysis                                                              | Irish Journal of Medical Science                                                                                             | 2022 | 191     |        | S223-S224 | Comparación equivocada         |
| Parmar, H and Edwards, L and Phillips, R H and Allen, L and Lightman, S L                                                                                                                                                      | Orchiectomy versus long-acting D-Trp-6-LHRH in advanced prostatic cancer                                                                                              | British journal of urology                                                                                                   | 1987 | 59      | 3      | 248-254   | Comparación equivocada         |
| MD, Gil-Sierra and EJ, Alegre-Del Rey and de la Lastra-Romero C, Alarcon and M, Sánchez-Hidalgo                                                                                                                                | Use of docetaxel in low- and high-burden metastatic hormone-sensitive prostate cancer: A systematic review and assessment of subgroup analyses.                       | Journal of oncology pharmacy practice : official publication of the International Society of Oncology Pharmacy Practitioners | 2021 | 27      | 7      | 1743-1750 | Tratamiento equivocado         |
| S, Roy and R, Sayyid and F, Saad and Y, Sun and K, Lajkosz and M, Ong and Z, Klaassen and S, Malone and                                                                                                                        | Addition of Docetaxel to Androgen Receptor Axis-targeted Therapy and Androgen Deprivation Therapy in Metastatic Hormone-                                              | European urology oncology                                                                                                    | 2022 | 5       | 5      | 494-502   | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Título                                                                                                                                                                                                                              | Revista                                                                                               | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| DE, Spratt and CJD, Wallis and SC, Morgan                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | sensitive Prostate Cancer: A Network Meta-analysis.                                                                                                                                                                                 |                                                                                                       |      |         |        |           |                                |
| NCT00004054                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Hormone Therapy Plus Radiation Therapy With or Without Combination Chemotherapy in Treating Patients With Prostate Cancer                                                                                                           | <a href="https://clinicaltrials.gov/show/NCT00004054">https://clinicaltrials.gov/show/NCT00004054</a> | 1999 |         |        |           | Tipo de publicación equivocada |
| Baydoun, A and Sun, Y and Sandler, H M and Bolla, M and Nabid, A and Denham, J W and Jia, A Y and Zaorsky, N G and Garcia, J and Brown, J and Jackson, W C and Dess, R T and Efsthathiou, J A and Feng, F Y and Maingon, P and Steigler, A and Souhami, L and Berlin, A and Kishan, A U and Spratt, D E                                                                                                                                                                                                                                                                                                                                                                                                          | Efficacy of Bicalutamide Monotherapy in Prostate Cancer: A Network Meta-Analysis of 10 Randomized Trials                                                                                                                            | International Journal of Radiation Oncology Biology Physics                                           | 2022 | 114     | 3      | e211-e212 | Tipo de publicación equivocada |
| G, Attard and L, Murphy and NW, Clarke and W, Cross and RJ, Jones and CC, Parker and S, Gillessen and A, Cook and C, Brawley and CL, Amos and N, Atako and C, Pugh and M, Buckner and S, Chowdhury and Z, Malik and JM, Russell and C, Gilson and H, Rush and J, Bowen and A, Lydon and I, Pedley and JM, O'Sullivan and A, Birtle and J, Gale and N, Srihari and C, Thomas and J, Tanguay and J, Wagstaff and P, Das and E, Gray and M, Alzoueb and O, Parikh and A, Robinson and I, Syndikus and J, Wylie and A, Zarkar and G, Thalmann and de Bono JS and DP, Dearnaley and MD, Mason and D, Gilbert and RE, Langley and R, Millman and D, Matheson and MR, Sydes and LC, Brown and MKB, Parmar and ND, James | Abiraterone acetate and prednisolone with or without enzalutamide for high-risk non-metastatic prostate cancer: a meta-analysis of primary results from two randomised controlled phase 3 trials of the STAMPEDE platform protocol. | Lancet (London, England)                                                                              | 2022 | 399     | ####   | 447-460   | Tratamiento equivocado         |

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| Schostak, M and Bögemann, M and Smith, M R and Shore, N D and Tammela, T L J and Ulys, A and Vjaters, E and Polyakov, S and Jievaltas, M and Luz, M and Alekseev, B and Kuss, I and Le Berre, M.-A. and Snapir, A and Sarapohja, T and Fizazi, K                                                                                           | Efficacy and safety of darolutamide in patients with nonmetastatic castration-resistant prostate cancer (nmCRPC) and a prostate-specific antigen doubling time (PSADT) > and ≤ 6 months | Oncology Research and Treatment                                                              | 2022 | 45      |        | 104-104        | Tipo de publicación equivocada |
| Ohlmann, C and Armstrong, A and Gratzke, C and Sugg, J and Ganguli, A and Dornstauder, E and Groß-Langenhoff, M and Brauner, R and Stenzl, A                                                                                                                                                                                               | An adjusted indirect treatment comparison (ITC) of enzalutamide (ENZ) versus docetaxel (DOC) for metastatic hormone-sensitive prostate cancer (mHSPC)                                   | Oncology Research and Treatment                                                              | 2022 | 45      |        | 108-108        | No se encuentra texto completo |
| A, Ramos-Esquivel and C, Fernández and Z, Zeledón                                                                                                                                                                                                                                                                                          | Androgen-deprivation therapy plus chemotherapy in metastatic hormone-sensitive prostate cancer. A systematic review and meta-analysis of randomized clinical trials.                    | Urologic oncology                                                                            | 2016 | 34      | 8      | 335.e9-335.e19 | Tratamiento equivocado         |
| C, Ciccarese and R, Iacovelli and CN, Sternberg and S, Gillesen and G, Tortora and K, Fizazi                                                                                                                                                                                                                                               | Triplet therapy with androgen deprivation, docetaxel, and androgen receptor signalling inhibitors in metastatic castration-sensitive prostate cancer: A meta-analysis.                  | European journal of cancer (Oxford, England : 1990)                                          | 2022 | 173     |        | 276-284        | Tratamiento equivocado         |
| MJ, Morris and G, Heller and DW, Hillman and O, Bobek and C, Ryan and ES, Antonarakis and AH, Bryce and O, Hahn and H, Beltran and AJ, Armstrong and L, Schwartz and LD, Lewis and JH, Beumer and B, Langevin and EC, McGary and PT, Mehan and A, Goldkorn and BJ, Roth and H, Xiao and C, Watt and ME, Taplin and S, Halabi and EJ, Small | Randomized Phase III Study of Enzalutamide Compared With Enzalutamide Plus Abiraterone for Metastatic Castration-Resistant Prostate Cancer (Alliance A031201 Trial).                    | Journal of clinical oncology : official journal of the American Society of Clinical Oncology | 2023 | 41      | 18     | 3352-3362      | Tratamiento equivocado         |
| Freedland, S J and de Almeida Luz, M and De Giorgi, U and Gleave, M and Gotto, G T and Pieczonka, C M and Haas, G P and Kim, C S and Ramirez-                                                                                                                                                                                              | Improved Outcomes with Enzalutamide in Biochemically Recurrent Prostate Cancer                                                                                                          | New England journal of medicine                                                              | 2023 | 389     | 16     | 1453-1465      | Población equivocada           |



| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Título                                                                                                                                                                            | Revista                                                                                                            | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Backhaus, M and Rannikko, A and al., et                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                   |                                                                                                                    |      |         |        |           |                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Active Surveillance, Radical Prostatectomy, or Radiation Therapy in Treating Patients With Localized Prostate Cancer                                                              | Active Monitoring, Radical Prostatectomy, or Radiation Therapy in Treating Patients With Localized Prostate Cancer | 2008 |         |        |           | Tipo de publicación equivocada |
| M, Hussain and B, Tombal and F, Saad and K, Fizazi and CN, Sternberg and ED, Crawford and N, Shore and E, Kopyltsov and AR, Kalebasty and M, Bögemann and D, Ye and F, Cruz and H, Suzuki and S, Kapur and S, Srinivasan and F, Verholen and I, Kuss and H, Joensuu and MR, Smith                                                                                                                                                                                                                                                                                                               | Darolutamide Plus Androgen-Deprivation Therapy and Docetaxel in Metastatic Hormone-Sensitive Prostate Cancer by Disease Volume and Risk Subgroups in the Phase III ARASENS Trial. | Journal of clinical oncology : official journal of the American Society of Clinical Oncology                       | 2023 | 41      | 20     | 3595-3607 | Tratamiento equivocado         |
| L, Emmett and S, Subramaniam and M, Crumbaker and A, Nguyen and AM, Joshua and A, Weickhardt and ST, Lee and S, Ng and RJ, Francis and JC, Goh and DA, Pattison and TH, Tan and ID, Kirkwood and C, Gedye and NK, Rutherford and S, Sandhu and AR, Kumar and D, Pook and S, Ramdave and DP, Nadebaum and M, Voskoboinik and AD, Redfern and W, Macdonald and L, Krieger and G, Schembri and W, Chua and P, Lin and L, Horvath and P, Bastick and P, Butler and AY, Zhang and S, Yip and H, Thomas and A, Langford and MS, Hofman and M, McJannett and AJ, Martin and MR, Stockler and ID, Davis | [(177)Lu]Lu-PSMA-617 plus enzalutamide in patients with metastatic castration-resistant prostate cancer (ENZA-p): an open-label, multicentre, randomised, phase 2 trial.          | The Lancet. Oncology                                                                                               | 2024 | 25      | 5      | 563-571   | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Título                                                                                                                                                                                                                                                | Revista                                                                                        | Año  | Volumen | Número | Páginas             | Razón de exclusión             |
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| L, Emmett and S, Subramaniam and M, Crumbaker and AM, Joshua and S, Sandhu and A, Nguyen and A, Weickhardt and ST, Lee and S, Ng and RJ, Francis and JC, Goh and DA, Pattison and TH, Tan and ID, Kirkwood and C, Gedye and NK, Rutherford and ASR, Kumar and D, Pook and S, Ramdave and DP, Nadebaum and M, Voskoboynik and AD, Redfern and W, Macdonald and L, Krieger and G, Schembri and W, Chua and P, Lin and L, Horvath and P, Bastick and P, Butler and AY, Zhang and M, McJannett and H, Thomas and A, Langford and MS, Hofman and AJ, Martin and ID, Davis and MR, Stockler | Overall survival and quality of life with [(177)Lu]Lu-PSMA-617 plus enzalutamide versus enzalutamide alone in metastatic castration-resistant prostate cancer (ENZA-p): secondary outcomes from a multicentre, open-label, randomised, phase 2 trial. | The Lancet. Oncology                                                                           | 2025 | 26      | 3      | 291-299             | Comparación equivocada         |
| F, Zengerling and JJ, Jakob and S, Schmidt and JJ, Meerpohl and A, Blümle and C, Schmucker and B, Mayer and F, Kunath                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Degarelix for treating advanced hormone-sensitive prostate cancer.                                                                                                                                                                                    | The Cochrane database of systematic reviews                                                    | 2021 | 8       | 8      | CD012548 - CD012548 | Comparación equivocada         |
| G, Attard and M, Borre and H, Gurney and Y, Lorient and C, Andresen-Daniil and R, Kalleda and T, Pham and ME, Taplin                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Abiraterone Alone or in Combination With Enzalutamide in Metastatic Castration-Resistant Prostate Cancer With Rising Prostate-Specific Antigen During Enzalutamide Treatment.                                                                         | Journal of clinical oncology : official journal of the American Society of Clinical Oncology   | 2018 | 36      | 25     | 2639-2646           | Comparación equivocada         |
| M, Hussain and M, Kocherginsky and N, Agarwal and N, Adra and J, Zhang and CJ, Paller and J, Picus and ZR, Reichert and RZ, Szmulewitz and ST, Tagawa and TM, Kuzel and LA, Bazzi and S, Daignault-Newton and YE, Whang and R, Dreicer and RD, Stephenson and MB, Rettig                                                                                                                                                                                                                                                                                                              | Abiraterone, Olaparib, or Abiraterone + Olaparib in First-Line Metastatic Castration-Resistant Prostate Cancer with DNA Repair Defects (BRCAAway).                                                                                                    | Clinical cancer research : an official journal of the American Association for Cancer Research | 2024 | 30      | 19     | 4318-4328           | Tipo de publicación equivocada |

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| and D, Shevrin and T, Gerke and AM, Chinnaiyan and ES, Antonarakis                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                 |                                         |      |         |        |               |                                |
| L, Zhen and W, Juan and F, Tianrui and C, Yuliang and Z, Zhien and Z, Yi and Y, Weigang and C, Fenghong                                                                                                                                                                                                                                                              | A net-work meta-analysis of the cardiac safety for next-generation hormonal agents in treating castration-resistant prostate cancer: How to choose drugs appropriately?                                                                                         | Critical reviews in oncology/hematology | 2024 | 196     |        | 104273-104273 | Desenlace equivocado           |
| F, Saad and de Bono J and N, Shore and K, Fizazi and Y, Lorient and M, Hirmand and B, Franks and GP, Haas and HI, Scher                                                                                                                                                                                                                                              | Efficacy outcomes by baseline prostate-specific antigen quartile in the AFFIRM trial.                                                                                                                                                                           | European urology                        | 2015 | 67      | 2      | 223-230       | Comparación equivocada         |
| CJ, Ryan and MR, Smith and Fizazi, K and Saad, F and PF, Mulders and CN, Sternberg and Miller, K and CJ, Logothetis and ND, Shore and EJ, Small and Carles, J and TW, Flaig and ME, Taplin and CS, Higano and P, de Souza and JS, de Bono and TW, Griffin and P, De Porre and MK, Yu and YC, Park and Li, J and Kheoh, T and Naini, V and Molina, A and DE, Rathkopf | Abiraterone acetate plus prednisone versus placebo plus prednisone in chemotherapy-naïve men with metastatic castration-resistant prostate cancer (COU-AA-302): final overall survival analysis of a randomised, double-blind, placebo-controlled phase 3 study |                                         |      |         | 1474   |               | Tipo de publicación equivocada |
| HY, Lee and HL, Chen and JY, Teoh and TC, Chen and SY, Hao and HY, Tsai and WH, Huang and YS, Juan and HM, Cheng and HM, Chang                                                                                                                                                                                                                                       | Abiraterone and enzalutamide had different adverse effects on the cardiovascular system: a systematic review with pairwise and network meta-analyses.                                                                                                           | Prostate cancer and prostatic diseases  | 2021 | 24      | 1      | 244-252       | Desenlace equivocado           |
| S, Satapathy and BR, Mittal and A, Sood                                                                                                                                                                                                                                                                                                                              | Visceral Metastases as Predictors of Response and Survival Outcomes in Patients of Castration-Resistant Prostate Cancer Treated With 177Lu-Labeled Prostate-Specific Membrane Antigen Radioligand Therapy: A Systematic Review and Meta-analysis.               | Clinical nuclear medicine               | 2020 | 45      | 12     | 935-942       | Comparación equivocada         |
| EJ, Lehrer and R, Singh and M, Wang and VM, Chinchilli and DM, Trifiletti and P, Ost and S, Siva and MB, Meng and L, Tchelebi and NG, Zaorsky                                                                                                                                                                                                                        | Safety and Survival Rates Associated With Ablative Stereotactic Radiotherapy for Patients With Oligometastatic Cancer: A Systematic Review and Meta-analysis.                                                                                                   | JAMA oncology                           | 2021 | 7       | 1      | 92-106        | Población equivocada           |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                     | Título                                                                                                                                              | Revista                                                                            | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| H, Zhang and P, Xin and YX, Zhang                                                                                                                                                                                                                                                                                                                                                                                         | [Efficacy and safety of the 177Lu-PSMA-617 therapy in the treatment of metastatic castration-resistant prostate cancer: A meta-analysis].           | Zhonghua nan ke xue = National journal of andrology                                | 2021 | 27      | 1      | 63-69   | No se encuentra texto completo |
| SAA, Naqvi and MU, Anjum and A, Bibi and MA, Khan and KZR, Khakwani and H, He and M, Imran and SZ, Kazmi and A, Raina and EK, Cobran and R, Bryan Rumble and TK, Oliver and N, Agarwal and Y, Zakharia and ME, Taplin and O, Sartor and P, Singh and JJ, Orme and DS, Childs and RA, Parikh and R, Garje and MH, Murad and AH, Bryce and IB, Riaz                                                                         | Systemic treatment options for metastatic castration resistant prostate cancer: A living systematic review.                                         | medRxiv : the preprint server for health sciences                                  | 2025 |         |        |         | Comparación equivocada         |
| H, Uemura and K, Kobayashi and A, Yokomizo and S, Hinotsu and S, Horie and Y, Kakehi and S, Naito and N, Nonomura and O, Ogawa and M, Oya and K, Suzuki and A, Saito and S, Uno and H, Akaza                                                                                                                                                                                                                              | Enzalutamide + androgen deprivation therapy (ADT) versus flutamide + ADT in Japanese men with castration-resistant prostate cancer: AFTERCAB study. | BJUI compass                                                                       | 2022 | 3       | 1      | 26-36   | Población equivocada           |
| B, Tombal and A, Choudhury and F, Saad and E, Gallardo and A, Soares and Y, Loriot and R, McDermott and A, Rodriguez-Vida and P, Isaacsson Velho and F, Nolè and F, Cruz and T, Roumeguere and G, Daugaard and R, Yamamura and E, Bompas and P, Maroto and F, Gomez Veiga and I, Skoneczna and da Trindade K, Martins and F, Mavignier Carcano and F, Lecouvet and C, Coens and C, Poncet and B, Fournier and S, Gillesen | Enzalutamide plus radium-223 in metastatic castration-resistant prostate cancer: results of the EORTC 1333/PEACE-3 trial.                           | Annals of oncology : official journal of the European Society for Medical Oncology | 2025 |         |        |         | Comparación equivocada         |
| D, Sentana-Lledo and X, Chu and DF, Jarrard and MA,                                                                                                                                                                                                                                                                                                                                                                       | Patient-reported Quality of Life and Survival Outcomes in Prostate Cancer: Analysis of the                                                          | European urology oncology                                                          | 2025 | 8       | 1      | 29-37   | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                              | Título                                                                                                                                                                                              | Revista                                                                         | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Carducci and RS, DiPaola and LI, Wagner and D, Cella and CJ, Sweeney and AK, Morgans                                                                                                                               | ECOG-ACRIN E3805 Chemohormonal Androgen Ablation Randomized Trial (CHAARTED).                                                                                                                       |                                                                                 |      |         |        |             |                                |
| S, Satapathy and CK, Das and S, Goyal and A, Sood and K, Periasamy and P, Aggarwal and K, Preet and SK, Singh and RS, Mavuduru and GS, Bora and AP, Sharma and G, Prakash and R, Kumar and H, Singh and BR, Mittal | (177)Lu-PSMA-617 Consolidation Therapy After Docetaxel in Patients with Synchronous High-Volume Metastatic Hormone-Sensitive Prostate Cancer: A Randomized, Phase 2 Trial.                          | Journal of nuclear medicine : official publication, Society of Nuclear Medicine | 2025 |         |        |             | Población equivocada           |
| F, Zhang and Z, Luo and Q, Xue and X, Guo and Q, Fu and Y, Jiao and W, Zhang and Y, Xiong and PA, Alisha and UA, Okoli and G, Zhang                                                                                | The efficacy of abiraterone in metastatic hormone-sensitive prostate cancer: a stratified meta-analysis based on subgroups of low or high disease volume and reconstructed individual patient data. | Expert review of anticancer therapy                                             | 2025 |         |        |             | No se encuentra texto completo |
| D'Agostino, F and Iacovelli, R and Ciccarese, C and Maratta, M G and Cigliola, A and Stefani, A and Anghelone, A and Sparagna, I and Strusi, A and Arduini, D and Bria, E and Tortora, G                           | PARP-INHIBITORS AS FIRST-LINE THERAPY FOR METASTATIC CASTRATION-RESISTANT PROSTATE CANCER AFTER DOCETAXEL IN THE CASTRATION-SENSITIVE DISEASE                                                       | Tumori                                                                          | 2022 | 108     | 4      | 100-100     | Tipo de publicación equivocada |
| Riaz, I B and Naqvi, S A A and He, H and Asghar, N and Siddiqi, R and Khakwani, K Z R and Liu, H and Hussain, S A and Singh, P and Murad, M and Bryce, A H                                                         | 1417P Mixed treatment comparisons evaluating contemporary therapies in metastatic castration sensitive prostate cancer (mCSPC): A living systematic review                                          | Annals of Oncology                                                              | 2022 | 33      |        | S1193-S1193 | Tipo de publicación equivocada |
| Gutta, D and Shah, R and Kalsey, M S and Gautam, R and Rai, M K                                                                                                                                                    | CO101 A Systematic Literature Review of Randomized Controlled Trials Reporting Efficacy and Safety of Treatments in Patients with Advanced Prostate Cancer in Asian Countries                       | Value in Health                                                                 | 2022 | 25      | 7      | S323-S323   | Tipo de publicación equivocada |
| Kumar, N                                                                                                                                                                                                           | ARASENS Trial: Should darolutamide now be added to androgen-deprivation therapy and docetaxel in patients with metastatic, hormone-sensitive prostate cancer?                                       | Indian Journal of Urology                                                       | 2022 | 38      | 3      | 238-239     | Tipo de publicación equivocada |
| Francis, P and Matthew, S R and Maha, H and Fred, S and Karim, F and Cora, S N and David, C E and Evgeny, K and                                                                                                    | Overall survival following treatment with darolutamide plus androgen-deprivation therapy and docetaxel for metastatic hormone-sensitive prostate cancer: primary                                    | Asia-Pacific Journal of Clinical Oncology                                       | 2022 | 18      |        | 76-76       | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                  | Título                                                                                                                                                                                                                                                          | Revista                                         | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| Francis, P and Fred, S and Andrew, A and Antoine, T.-V. and Mototsugu, O and Eugenia, L and Giuseppe, P and Juliana, D M and Gustavo, G and Cagatay, A and Niven, M and Emma, B and Friederike, S and Young, J J and Mikio, S and Christian, P and Elizabeth, H and Chintu, D and Jinyu, K and Noel, C | PROpel: Phase III trial of olaparib and abiraterone vs placebo and abiraterone as firstline (1L) therapy for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC)                                                                        | Asia-Pacific Journal of Clinical Oncology       | 2022 | 18      |        | 80-80   | Tipo de publicación equivocada |
| Uemura, H and Arai, G and Uemura, H and Suzuki, H and Aoyama, J and Hatayama, T and Ito, M and Lefresne, F and McCarthy, S and Mundle, S and He, J and Chi, K N                                                                                                                                        | Safety and efficacy of apalutamide in Japanese patients with metastatic castration-sensitive prostate cancer receiving androgen deprivation therapy: Final report for the Japanese subpopulation analysis of the randomized, placebo-controlled, phase III TITA | International Journal of Urology                | 2022 | 29      | 6      | 533-540 | Tipo de publicación equivocada |
| Naqvi, S A A and Riaz, Z B and Riaz, A and Islam, M and Siddiqi, R and Ikram, W and Zafar, M D B and Singh, P and Riaz, I B and Bryce, A H                                                                                                                                                             | Indirect comparisons of triplet therapy as compared to novel hormonal therapy doublets in patients with metastatic castration sensitive prostate cancer                                                                                                         | Journal of Clinical Oncology                    | 2022 | 40      | 16     |         | Tipo de publicación equivocada |
| Kortbeek, K and Rottey, S                                                                                                                                                                                                                                                                              | PARP inhibitors in metastatic prostate cancer: a systematic review                                                                                                                                                                                              | Tijdschrift voor Geneeskunde en Gezondheidszorg | 2022 | 78      | 5      |         | No se encuentra texto completo |
| Boccardo, F and Barichello M FAU - Battaglia, Michele and Battaglia M FAU - Carmignani, Giorgio and Carmignani G FAU - Comeri, Giancarlo and Comeri G FAU - Ferraris, Valentino and Ferraris V FAU - Lilliu, Sergio and Lilliu S FAU - Montefiore, Franco and                                          | Bicalutamide monotherapy versus flutamide plus goserelin in prostate cancer: updated results of a multicentric trial. PG - 481-90                                                                                                                               |                                                 |      |         | 302    |         | Tipo de publicación equivocada |

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| Montefiore F FAU - Portoghese, Filippo and Portoghese F FAU - Cortellini, Pietro and Cortellini P FAU - Rigatti, Patrizio and Rigatti P FAU - Usai, Enzo and Usai E FAU - Rubagotti, Alessandra and Group, Rubagotti A C N - Italian Prostate Cancer                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                 |                                                                                              |      |         |        |           |                                |
| Lunglmayr, G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | A multicenter trial comparing the luteinizing hormone releasing hormone analog Zoladex, with Zoladex plus flutamide in the treatment of advanced prostate cancer. The International Prostate Cancer Study Group | European urology                                                                             | 1990 | 18      |        | 28-29     | Tipo de publicación equivocada |
| HL, Rush and L, Murphy and AK, Morgans and NW, Clarke and AD, Cook and G, Attard and A, Macnair and DP, Dearnaley and CC, Parker and JM, Russell and S, Gillessen and D, Matheson and R, Millman and CD, Brawley and C, Pugh and JS, Tanguay and RJ, Jones and J, Wagstaff and S, Rudman and JM, O'Sullivan and J, Gale and A, Birtle and A, Protheroe and E, Gray and C, Perna and S, Tolan and N, McPhail and ZI, Malik and S, Vengalil and D, Fackrell and P, Hoskin and MR, Sydes and S, Chowdhury and DC, Gilbert and MKB, Parmar and ND, James and RE, Langley | Quality of Life in Men With Prostate Cancer Randomly Allocated to Receive Docetaxel or Abiraterone in the STAMPEDE Trial.                                                                                       | Journal of clinical oncology : official journal of the American Society of Clinical Oncology | 2022 | 40      | 8      | 825-836   | Tratamiento equivocado         |
| Shore, N D and Iguchi, T and Villers, A and Alcaraz, A and Gomez-Veiga, F and Stenzl, A and Azad, A A and Alekseev, B and Petrylak, D P and Szmulewitz, R Z and al., et                                                                                                                                                                                                                                                                                                                                                                                              | Enzalutamide in metastatic hormone-sensitive prostate cancer patients who received prior antiandrogen therapy: post hoc analysis of arches                                                                      | Journal of urology                                                                           | 2021 | 206     |        | e585-e585 | Tipo de publicación equivocada |

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| Saad, M and Umbas, R and Chiong, E and Kanesvaran, R                                                                                                                                                                                                                                                     | Efficacy and safety of therapies for advanced prostate cancer in Asia: Evidence from a systematic literature review                                                                                                                                              | Therapeutic Advances in Medical Oncology | 2022 | 14      |        |         | Diseño de estudio equivocado   |
| Damber, J E and Tammela, T L and Iversen, P and Abrahamsson, P A and Boccon-Gibod, L and Olesen, T K and van der Meulen, E and Persson, B E                                                                                                                                                              | The effect of baseline testosterone on the efficacy of degarelix and leuprolide: further insights from a 12-month, comparative, phase III study in prostate cancer patients                                                                                      | Urology                                  | 2012 | 80      | 1      | 174-180 | Tipo de publicación equivocada |
| Kibel, A S and Gleave, M and Brookman-May, S D and Kim, W and Evans, C P and Efsthathiou, E and Kantoff, P W and Ross, A and Shore, N D and Briganti, A and Hadaschik, B A and Heidenreich, A and Rooney, O B and Tian, S K and Wetherhold, L and Xu, W and Parsons, J K and Yeruva, K and Taplin, M.-E. | PROTEUS: A randomized, double-blind, placebo (PBO)-controlled, phase 3 trial of apalutamide (APA) plus androgen deprivation therapy (ADT) versus PBO plus ADT prior to radical prostatectomy (RP) in patients (pts) with localized or locally advanced high-risk | Journal of Clinical Oncology             | 2022 | 40      | 6      |         | Tipo de publicación equivocada |
| Saad, F and Armstrong, A J and Thiery-Vuillemin, A and Oya, M and Lored, E and Procopio, G and De Menezes, J J and Girotto, G C and Arslan, C and Mehra, N and al., et                                                                                                                                   | PROpel: phase III trial of olaparib (ola) and abiraterone (abi) versus placebo (pbo) and abi as first-line (1L) therapy for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC)                                                          | Journal of clinical oncology             | 2022 | 40      | 6      |         | Tipo de publicación equivocada |
| Yokomizo, A and Morokuma, F and Eto, M and Shiota, M and Matsuyama, H and Matsumoto, H and Kamoto, T and Terada, N and Kawahara, K and Enokida, H and Tatarano, S and Fujimoto, N and Higashijima, K and Sakai, H and Hakariya, T and Igawa, T and Suekane, S and Kamba, T and Sugiyama, Y and Naito, S  | Randomized controlled trial of GnRH antagonist monotherapy versus GnRH agonist plus bicalutamide (CAB) for patients with metastatic hormone-sensitive prostate cancer (mHSPC) (KYUCOG-1401)                                                                      | Journal of Clinical Oncology             | 2022 | 40      | 6      |         | Tipo de publicación equivocada |
| Izumi, K and Shima, T and Mita, K and Kato, Y and Kamiyama, M and Inoue, S                                                                                                                                                                                                                               | Enzalutamide versus abiraterone plus prednisolone before chemotherapy for Japanese castration-resistant prostate cancer                                                                                                                                          | Journal of Clinical Oncology             | 2022 | 40      | 6      |         | Población equivocada           |



| Autor                                                                                                                                                                                                                 | Título                                                                                                                                                                                                                                                         | Revista                                    | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| Riaz, I B and Ahmed Naqvi, S A and Ikram, W and Siddiqi, R and Asghar, N and Rubab Khakwani, K Z and Khalid, A and Hussain, S A and Singh, P and Bryce, A H                                                           | First-line treatment options in metastatic castration-sensitive prostate cancer: A systematic review and network meta-analysis                                                                                                                                 | Journal of Clinical Oncology               | 2022 | 40      | 6      |         | Tipo de publicación equivocada |
| Ahmed Naqvi, S A and Bin Zafar, M D and Islam, M and Ikram, W and Raina, A and Singh, P and Riaz, I B and Bryce, A H                                                                                                  | Differential efficacy of PARP inhibitors in metastatic castration-resistant prostate cancer with DNA repair defects: A systematic review and meta-analysis                                                                                                     | Journal of Clinical Oncology               | 2022 | 40      | 6      |         | Tipo de publicación equivocada |
| Ahmed Naqvi, S A and Riaz, Z B and Riaz, A and Islam, M and Siddiqi, R and Ikram, W and Jafar, M A and Singh, P and Ravi, P K and Riaz, I B and Bryce, A H                                                            | Triplet therapy in metastatic castration-sensitive prostate cancer: A systematic review and meta-analysis                                                                                                                                                      | Journal of Clinical Oncology               | 2022 | 40      | 6      |         | Tipo de publicación equivocada |
| James, N D and Clarke, N W and Cook, A and Ali, A and Hoyle, A P and Attard, G and Brawley, C D and Chowdhury, S and Cross, W R and Dearnaley, D P and al., et                                                        | Abiraterone acetate plus prednisolone for metastatic patients starting hormone therapy: 5-year follow-up results from the STAMPEDE randomised trial (NCT00268476)                                                                                              | International journal of cancer            | 2022 | 151     | 3      | 422-434 | Población equivocada           |
|                                                                                                                                                                                                                       | Phase 3 study of 177Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION)                                                                                                                                                      | Clinical advances in hematology & oncology | 2021 | 19      | 8      | 3-5     | Tipo de publicación equivocada |
| Thiery-Vuillemin, A and J, de Bono and Hussain, M and Roubaud, G and Procopio, G and Shore, N and Fizazi, K and G, Dos Anjos and Gravis, G and JY, Joung and Matsubara, N and Castellano, D and Degboe, A and Gresty, | Pain and health-related quality of life with olaparib versus physician's choice of next-generation hormonal drug in patients with metastatic castration-resistant prostate cancer with homologous recombination repair gene alterations (PROfound): an open-la |                                            |      |         | 1474   |         | Tipo de publicación equivocada |

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| Cathomas, R and Procopio, G and Hayoz, S and Kremer, E A and Kienle, D and Caffo, O and Lorente, D and Pedrazzini, A and Roubaud, G and Nenán, S and Omlin, A G and Buttiglieri, C and Pereira Mestre, R J and Ribí, K and Gillesen, S | LBA26 Darolutamide maintenance in metastatic castration resistant prostate cancer (mCRPC) previously treated with novel hormonal agents (NHA) and non-progressive disease after subsequent treatment with a taxane: A randomized double-blind placebo-controlle | Annals of Oncology                                  | 2021 | 32      |        | S1301-S1302 | Tipo de publicación equivocada |
| Kyriakopoulos, C and Chen, Y-H and Duan, F and Jeraaj, R and Luo, J and Antonarakis, E S and Liu, G and Carducci, M A                                                                                                                  | Cabazitaxel with abiraterone versus abiraterone alone randomized trial for extensive disease following docetaxel: the CHAARTED 2 Trial: a trial of the ECOG-ACRIN Cancer Research Group (EA8153)                                                                | Journal of clinical oncology                        | 2019 | 37      |        |             | Tipo de publicación equivocada |
| Iguchi, T and Tamada, S and Kato, M and Yasuda, S and Yamasaki, T and Nakatani, T                                                                                                                                                      | Enzalutamide versus flutamide for castration-resistant prostate cancer after combined androgen blockade therapy with bicalutamide: study protocol for a multicenter randomized phase II trial (the OCUU-CRPC study). PG - 339 LID - 10.1186/s12885-019-5526-3   |                                                     |      |         | 1471   |             | Tipo de publicación equivocada |
| Shen, Y J and Bian, X J and Xie, H Y and Zhu, Y and Zhang, H L and Dai, B and Zhang, S L and Yao, X D and Ye, D W                                                                                                                      | Docetaxel plus prednisone versus mitoxantrone plus prednisone as first-line chemotherapy for metastatic hormone-refractory prostate cancer: long-term effects and safety                                                                                        | Zhonghua wai ke za zhi [Chinese journal of surgery] | 2012 | 50      | 6      | 539-542     | Diseño de estudio equivocado   |
| Teply, B A and Qiu, F and Antonarakis, E S and Carducci, M A and Denmeade, S R                                                                                                                                                         | Risk of development of visceral metastases subsequent to abiraterone vs placebo: an analysis of mode of radiographic progression in COU-AA-302                                                                                                                  | Prostate                                            | 2019 | 79      | 8      | 929-933     | Diseño de estudio equivocado   |
| Mishra, A                                                                                                                                                                                                                              | Benefit of cabazitaxel in previously treated metastatic castration-resistant prostate cancer; CARD trial                                                                                                                                                        | Indian journal of urology                           | 2020 | 36      | 4      | 329-330     | Tipo de publicación equivocada |
| Wang, L and Paller, C and Hong, H and Brawley, O and Alexander, G C                                                                                                                                                                    | Efficacy and safety of treatments for nonmetastatic castration-resistant prostate cancer: A matching-adjusted indirect comparison and network meta-analysis                                                                                                     | Pharmacoepidemiology and Drug Safety                | 2021 | 30      |        | 13-13       | Tipo de publicación equivocada |
| Wulfng, C and Castellano, D and Kramer, G and Eymard, J-C and De Bono, J and                                                                                                                                                           | CARD: cabazitaxel (CBZ) vs Abiraterone (ABI) or Enzalutamide (ENZ) in metastatic castration-resistant prostate cancer (mCRPC)                                                                                                                                   | Oncology research and treatment                     | 2020 | 43      |        | 224-225     | Tipo de publicación equivocada |

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| ND, James and FC, Ingleby and NW, Clarke and CL, Amos and G, Attard and CD, Brawley and S, Chowdhury and W, Cross and DP, Dearnaley and DC, Gilbert and S, Gillesen and RJ, Jones and RE, Langley and A, Macnair and ZI, Malik and MD, Mason and DJ, Matheson and R, Millman and CC, Parker and HL, Rush and JM, Russell and C, Au and AWS, Ritchie and RP, Mestre and I, Ahmed and AJ, Birtle and SJ, Brock and P, Das and VA, Ford and EK, Gray and RJ, Hughes and CB, Manetta and DB, McLaren and AD, Nikapota and JM, O'Sullivan and C, Perna and C, Peedell and AS, Protheroe and S, Sundar and JS, Tanguay and SP, Tolan and J, Wagstaff and JB, Wallace and JP, Wylie and A, Zarkar and MKB, Parmar and MR, Sydes | Docetaxel for Nonmetastatic Prostate Cancer: Long-Term Survival Outcomes in the STAMPEDE Randomized Controlled Trial.                                                                                 | JNCI cancer spectrum                      | 2022 | 6       | 4      |           | Tratamiento equivocado         |
| Haider, S and Dai, E and Sim, H and Balakrishnar, B and Descallar, J and Ding, P and Chua, W                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Systematic review and meta-analysis of treatment related toxicities from second-generation androgen receptor inhibitors in advanced prostate cancer                                                   | Asia-Pacific Journal of Clinical Oncology | 2020 | 16      |        | 121-121   | Tipo de publicación equivocada |
| Tombal, B F and Gomez-Veiga, F and Gomez-Ferrer, A and López-Campos, F and Ost, P and Roumeguere, T A and                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A Phase 2 Randomized Open-label Study of Oral Darolutamide Monotherapy Versus Androgen Deprivation Therapy in Men with                                                                                | European urology oncology                 | 2024 | 7       | 5      | 1051-1060 | Diseño de estudio equivocado   |

| Autor                                                                                                                                                                                                                                    | Título                                                                                                                                                                                                           | Revista                                                                            | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Herrera-Imbroda, B and D'Hondt, L A and Quivrin, M and Gontero, P and al., et                                                                                                                                                            | Hormone-sensitive Prostate Cancer (EORTC-GUCG 1532)                                                                                                                                                              |                                                                                    |      |         |        |           |                                |
| So, T H and Chiang, C L and Lam, T.-C. and Chan, F T and Choi, H                                                                                                                                                                         | What is the best first-line therapy for metastatic castration-sensitive prostate cancer in 2020: A network meta-analysis                                                                                         | Asia-Pacific Journal of Clinical Oncology                                          | 2020 | 16      |        | 5-5       | Tipo de publicación equivocada |
| Van Der Zande, K and Van Der Noort, V and Busard, M and Hamberg, P and Ras-van Spijk, S and De Feijter, J and Dezentje, V O and Tascilar, M and Houtsma, D and Beeker, A and al., et                                                     | First results from a randomized phase II study of cabazitaxel (CBZ) versus an androgen receptor targeted agent (ARTA) in patients with poor-prognosis castrationresistant prostate cancer (mCRPC)                | Journal of clinical oncology                                                       | 2021 | 39      | 15     |           | Tipo de publicación equivocada |
| Stenzl, A and Szmulewitz, R Z and Petrylak, D and Holzbeierlein, J and Villers, A and Azad, A and Alcaraz, A and Alekseev, B and Iguchi, T and Shore, N D and Gomez-Veiga, F and Rosbrook, B and Baron, B and Haas, G P and Armstrong, A | ARCHES: Efficacy of androgen deprivation therapy (ADT) with enzalutamide (ENZA) or placebo (PBO) in metastatic hormone-sensitive prostate cancer (mHSPC) by prior local and systemic treatment                   | European Urology Open Science                                                      | 2020 | 19      |        | e865-e866 | Tipo de publicación equivocada |
| Ternov Kvorning, K and Nolsøe, A B and Bratt, O and Fode, M and Lindberg, H and Kistorp, C and Palapattu, G and Klausen, T W and Sønksen, J and Østergren, P B                                                                           | Short term health-related quality-of-life in men with metastatic castration-resistant prostate cancer treated with first-line enzalutamide or abiraterone plus prednisone: A systematic review and meta-analysis | European Urology Open Science                                                      | 2020 | 19      |        | e869-e870 | Tipo de publicación equivocada |
| Sun, Y and Xie, L and Xu, T and Jakobsen, J S and Han, W and Sorensen, P S and Wang, X                                                                                                                                                   | Efficacy and safety of degarelix in patients with prostate cancer: results from a phase III study in China                                                                                                       | Asian journal of urology                                                           | 2020 | 7       | 3      | 301-308   | Tratamiento equivocado         |
| Berthold, D R and Pond, G R and de Wit, R and Eisenberger, M and Tannock, I F                                                                                                                                                            | Survival and PSA response of patients in the TAX 327 study who crossed over to receive docetaxel after mitoxantrone or vice versa                                                                                | Annals of oncology : official journal of the european society for medical oncology | 2008 | 19      | 10     | 1749-1753 | Diseño de estudio equivocado   |
| Iversen, P                                                                                                                                                                                                                               | Zoladex plus flutamide vs. orchidectomy for advanced prostatic cancer. Danish Prostatic Cancer Group (DAPROCA). PG - 41-4                                                                                        |                                                                                    |      |         | 302    |           | Tratamiento equivocado         |
| CC, Parker and NW, Clarke and AD, Cook and Kynaston, H and CN, Catton and WR,                                                                                                                                                            | Adding 6 months of androgen deprivation therapy to postoperative radiotherapy for prostate cancer: a comparison of short-                                                                                        |                                                                                    |      |         | 1474   |           | Tratamiento equivocado         |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Título                                                                                                                                                                                                                     | Revista                | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| Cross and PM, Petersen and RA, Persad and Saad, F and LC, Bower and Logue, J and Payne, H and Forcat, S and Goldstein, C and Murphy, C and Anderson, J and Barkati, M and DM, Bottomley and Branagan, J and Choudhury, A and PWM, Chung and Cogley, L and CL, Goh and Hoskin, P and Khoo, V and SC, Malone and Masters, L and SL, Morris and Nabid, A and AD, Ong and Raman, R and KL, Tarver and AC, Tree and Worthing, J and JP, Wylie and AM, Zarkar and WR, Parulekar and MKB, Parmar and MR, Sydes | course versus no androgen deprivation therapy in the RADICALS-HD randomised controlled trial. PG - 2405-2415 LID - S0140-6736(24)005                                                                                       |                        |      |         |        |         |                                |
| Wang, L and Paller, C and Hong, H and Alexander, C and Brawley, O                                                                                                                                                                                                                                                                                                                                                                                                                                       | CE3 COMPARATIVE EFFECTIVENESS OF SYSTEMATIC THERAPIES FOR METASTATIC CASTRATION-SENSITIVE PROSTATE CANCER: A PARAMETRIC SURVIVAL NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS                                     | Value in Health        | 2020 | 23      |        | S3-S3   | Tipo de publicación equivocada |
| WC, Jackson and HE, Hartman and RT, Dess and SR, Birer and PD, Soni and JWD, Hearn and ZR, Reichert and AU, Kishan and BA, Mahal and ZS, Zumsteg and JA, Efstathiou and Kaffenberger, S and TM, Morgan and Mehra, R and TN, Showalter and DA, Krauss and PL, Nguyen and MJ, Schipper and FY, Feng and HM, Sandler and PJ, Hoskin and 3rd, Roach M and DE, Spratt                                                                                                                                        | Addition of Androgen-Deprivation Therapy or Brachytherapy Boost to External Beam Radiotherapy for Localized Prostate Cancer: A Network Meta-Analysis of Randomized Trials. PG - 3024-3031 LID - 10.1200/JCO.19.03217 [doi] |                        |      |         | 1527   |         | Tratamiento equivocado         |
| Greenberger, B A and Zaorsky, N G and Den, R B                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Comparison of Radical Prostatectomy Versus Radiation and Androgen Deprivation Therapy Strategies as Primary Treatment for High-risk Localized Prostate Cancer: A Systematic Review and Meta-analysis                       | European Urology Focus | 2020 | 6       | 2      | 404-418 | Diseño de estudio equivocado   |

| Autor                                                                                                                                                                                                                                                                            | Título                                                                                                                                                                                                               | Revista                                    | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| Iguchi, T and Tamada, S and Kato, M and Yasuda, S and Machida, Y and Ohmachi, T and Ishii, K and Iwata, H and Yamamoto, S and Kanamaru, T and Morimoto, K and Hase, T and Tashiro, K and Harimoto, K and Deguchi, T and Adachi, T and Iwamoto, K and Takegaki, Y and Nakatani, T | Enzalutamide versus flutamide for castration-resistant prostate cancer after combined androgen blockade therapy with bicalutamide: the OCUU-CRPC study                                                               | International Journal of Clinical Oncology | 2020 | 25      | 3      | 486-494 | Población equivocada           |
| Chung, D Y and Kang, D H and Kim, J W and Kim, D K and Lee, J Y and Hong, C H and Cho, K S                                                                                                                                                                                       | Comparison of oncologic outcomes between two alternative sequences with abiraterone acetate and enzalutamide in patients with metastatic castration-resistant prostate cancer: A systematic review and meta-analysis | Cancers                                    | 2020 | 12      | 1      |         | Diseño de estudio equivocado   |
| Rashid, M and Ramesh, M and Shamshavali, K and Dang, A and Patel, H and Undela, K                                                                                                                                                                                                | Efficacy and safety of non-steroidal anti-androgens in patients with metastatic prostate cancer: Meta-analysis of randomized controlled trials                                                                       | Reviews on Recent Clinical Trials          | 2020 | 15      | 1      | 34-47   | No se encuentra texto completo |
| Jiang, D M and Wong, B and Morgans, A K and Sweeney, C and Fizazi, K and Chi, K N and Powles, T and Perlis, N and Kulkarni, G S and Sridhar, S S                                                                                                                                 | Improving quality of health-related quality of life (HRQOL) reporting in phase III randomized controlled trials (RCTs) of metastatic prostate cancer (mPC)                                                           | Journal of Clinical Oncology               | 2020 | 38      | 6      |         | Tipo de publicación equivocada |
| Cusano, E and Lee-Ying, R M and Boyne, D J and Brenner, D and Vaska, M                                                                                                                                                                                                           | Systemic therapy for nonmetastatic castrate-resistant prostate cancer (M0 CRPC): A systematic review and network meta-analysis (NMA)                                                                                 | Journal of Clinical Oncology               | 2020 | 38      | 6      |         | Tipo de publicación equivocada |
| Riaz, I B and Asghar, N and Lang, D K and Yao, Y and Riaz, A and Almutairi, A and Wang, Z and Abraham, I and Murad, M H and Kohli, M                                                                                                                                             | A systematic review and network meta-analysis of FDA approved treatment options in men with nonmetastatic, castration-resistant prostate cancer (M0CRPC)                                                             | Journal of Clinical Oncology               | 2020 | 38      | 6      |         | Tipo de publicación equivocada |
| Hird, A E and Magee, D E and Bhindi, B and Ye, X Y and Chandrasekar, T and Goldberg, H and Klotz, L and Fleshner, N and Satkunasivam, R and William,                                                                                                                             | Novel androgen receptor inhibitors in nonmetastatic castration-resistant prostate cancer: A network meta-analysis                                                                                                    | Journal of Clinical Oncology               | 2020 | 38      | 6      |         | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Título                                                                                                                                                                                       | Revista                              | Año  | Volumen | Número | Páginas | Razón de exclusión             |
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| Z and Klaassen, A and Wallis, C J D                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                              |                                      |      |         |        |         |                                |
| Wang, L and Paller, C and Hong, H and De Felice, A and Brawley, O and Alexander, C                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Comparative effectiveness and safety of systemic treatments for metastatic castration-sensitive prostate cancer: A parametric survival network meta-analysis of randomized controlled trials | Pharmacoepidemiology and Drug Safety | 2020 | 29      |        | 108-108 | Tipo de publicación equivocada |
| Riaz Sipra, Q U A and Riaz, I B and Asghar, N and Siddiqi, R and Hwang, S R and Husnain, M and Adil, S and Raina, A and Maheswari, D and Babiker, H M and Murad, M H and Singh, P and Bryce, A H                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Treatment of metastatic castration sensitive prostate cancer (mCSPC) by disease volume: A systematic review and a metaanalysis                                                               | Journal of Clinical Oncology         | 2020 | 38      | 15     |         | Tipo de publicación equivocada |
| Jahan, N and Mogollon-Duffo, F and Rehman, S and Singal, S and Hardwicke, F L                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Relative risk of HTN and major cardiovascular events associated with use of androgen receptor antagonists for nonmetastatic, castration-resistant prostate cancer                            | Journal of Clinical Oncology         | 2020 | 38      | 15     |         | Tipo de publicación equivocada |
| Kotake, T and Usami M FAU - Isaka, S and Isaka S FAU - Shimazaki, J and Shimazaki J FAU - Nakano, E and Nakano E FAU - Okuyama, A and Okuyama A FAU - Okajima, E and Okajima E FAU - Kanetake, H and Kanetake H FAU - Saitoh, Y and Saitoh Y FAU - Kumamoto, Y and Kumamoto Y FAU - Orikasa, S and Orikasa S FAU - Sakata, Y and Sakata Y FAU - Hosaka, M and Hosaka M FAU - Akaza, H and Akaza H FAU - Koiso, K and Koiso K FAU - Honma, Y and Honma Y FAU - Aso, Y and Aso Y FAU - Oishi, K and Oishi K FAU - Yoshida, O and Yoshida O FAU - Naitoh, S and Naitoh S FAU - Kumazawa, J and Kumazawa J FAU - Koyanagi, T and Koyanagi T FAU - Yachiku, S and Yachiku | [Clinical early phase II study of bicalutamide (Casodex) in patients with prostatic cancer]. PG - 157-68                                                                                     |                                      |      |         | 18     |         | Tratamiento equivocado         |

| Autor                                                                                                                                                                       | Título                                                                                                                                                                                                                                                            | Revista                                                     | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| S FAU - Shiraiwa, Y and Shiraiwa Y FAU - Tsukagoshi, S and Tsukagoshi, S                                                                                                    |                                                                                                                                                                                                                                                                   |                                                             |      |         |        |             |                                |
| Mottet, N and Peneau, M and Mazon, J J and Molin, V and Richaud, P                                                                                                          | Addition of radiotherapy to long-term androgen deprivation in locally advanced prostate cancer: an open randomised phase 3 trial                                                                                                                                  | European urology                                            | 2012 | 62      | 2      | 213-219     | Comparación equivocada         |
| Jahan, N and Rehman, S and Mogollon-Duffo, F and Ball, S and Wongsangsak, S and Tijani, L A                                                                                 | Efficacy of androgen receptor antagonists in combination with androgen deprivation therapy in nonmetastatic, castration-resistant prostate cancer: A systematic review and metaanalysis of published phase III randomized controlled trials                       | Journal of Clinical Oncology                                | 2020 | 38      | 15     |             | Tipo de publicación equivocada |
| Wongsangsak, S and Jahan, N and Hardwicke, F L                                                                                                                              | Safety and tolerance of androgen receptor antagonists in nonmetastatic, castration-resistant prostate cancer                                                                                                                                                      | Journal of Clinical Oncology                                | 2020 | 38      | 15     |             | Tipo de publicación equivocada |
| Pawson, A and Zukotynski, K                                                                                                                                                 | A systematic review of Lutetium-177 PSMA therapy in prostate cancer                                                                                                                                                                                               | BMC Proceedings                                             | 2020 | 14      |        |             | Tipo de publicación equivocada |
|                                                                                                                                                                             | A Phase-II, Randomized, Assessor-Blind, Controlled Trial Comparing the Occurrence of Cardiovascular Events in Patients With Prostate Cancer and Cardiovascular Risk Factors Receiving Degarelix or GnRH Agonist                                                   | <a href="https://clinicaltrials.gov">clinicaltrials.gov</a> | 2019 |         |        |             | Tipo de publicación equivocada |
| Denmeade, S R and Wang, H and Agarwal, N and Smith, D C and Schweizer, M T and Stein, M N and Assikis, V and Twardowski, P W and Flaig, T W and Szmulewitz, R Z and al., et | TRANSFORMER: a Randomized Phase II Study Comparing Bipolar Androgen Therapy Versus Enzalutamide in Asymptomatic Men With Castration-Resistant Metastatic Prostate Cancer                                                                                          | Journal of clinical oncology                                | 2021 | 39      | 12     | 1371-1382   | Tipo de publicación equivocada |
| Attard, G and Murphy, L and Clarke, N and Cross, W and Gillissen, S and Amos, C and Brawley, C and Jones, R and Pezaro, C and Malik, Z and al., et                          | LBA62 Comparison of abiraterone acetate and prednisolone (AAP) or combination enzalutamide (ENZ) + AAP for metastatic hormone sensitive prostate cancer (mHSPC) starting androgen deprivation therapy (ADT): overall survival (OS) results of 2 randomised phases | Annals of oncology                                          | 2022 | 33      |        | S1427-S1428 | Diseño de estudio equivocado   |
| Khalaf, D J and Annala, M and Taavitsainen, S and Finch, D L and Oja, C and Vergidis, J and Zulfiqar, M and Sunderland, K                                                   | Optimal sequencing of enzalutamide and abiraterone acetate plus prednisone in metastatic castration-resistant prostate                                                                                                                                            | The lancet. Oncology                                        | 2019 | 20      | 12     | 1730-1739   | Artículo general               |



| Autor                                                                                                                                                                                                                             | Título                                                                                                                                                                                                                     | Revista                      | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| and Azad, A A and Kollmannsberger, C K and al., et                                                                                                                                                                                | cancer: a multicentre, randomised, open-label, phase 2, crossover trial                                                                                                                                                    |                              |      |         |        |           |                                |
| Smith, M R and Saad, F and Chowdhury, S and Oudard, S and Hadaschik, B A and Graff, J N and Olmos, D and Mainwaring, P N and Lee, J Y and Uemura, H and De Porre, P and Smith, A and Zhang, K and Lopez-Gitlitz, A and Small, E J | Apalutamide (APA) and overall survival (OS) in patients (pts) with nonmetastatic castration-resistant prostate cancer (nmCRPC): Updated results from the phase III SPARTAN study                                           | Annals of Oncology           | 2019 | 30      |        | v325-v325 | Tipo de publicación equivocada |
| Uemura, H and Kobayashi, K and Yokomizo, A and Hinotsu, S and Horie, S and Kakehi, Y and Naito, S and Nonomura, N and Ogawa, O and Oya, M and al., et                                                                             | Enzalutamide plus androgen deprivation therapy (ADT) versus flutamide plus ADT in men with castration-resistant prostate cancer (CRPC): AFTERCAB                                                                           | Journal of clinical oncology | 2021 | 39      | 6      |           | Tipo de publicación equivocada |
| Chodak, G and Sharifi R FAU - Kasimis, B and Kasimis B FAU - Block, N L and Block NL FAU - Macramalla, E and Macramalla E FAU - Kennealey, G T and GT, Kennealey                                                                  | Single-agent therapy with bicalutamide: a comparison with medical or surgical castration in the treatment of advanced prostate carcinoma. PG - 849-55                                                                      |                              |      |         | 90     |           | Tratamiento equivocado         |
| Hussain, M H A and Kocherginsky, M and Agarwal, N and Adra, N and Zhang, J and Paller, C J and Picus, J and Reichert, Z R and Szmulewitz, R Z and Tagawa, S T and al., et                                                         | BRCAAway: a randomized phase 2 trial of abiraterone, olaparib, or abiraterone + olaparib in patients with metastatic castration-resistant prostate cancer (mCRPC) bearing homologous recombination-repair mutations (HRRm) | Journal of clinical oncology | 2024 | 42      | 4      |           | Tipo de publicación equivocada |
| Botto, H and Rouprêt M FAU - Mathieu, François and Mathieu F FAU - Richard, François and Richard, F                                                                                                                               | [Multicentre randomized trial comparing triptorelin medical castration versus surgical castration in the treatment of locally advanced or metastatic prostate cancer]. PG - 235-9                                          |                              |      |         | 1166   |           | Tipo de publicación equivocada |
| Shore, N and Saad, F and Hussain, M and Fizazi, K and Rathenborg, P and Demirhan, E and Modelska, K and Phung,                                                                                                                    | The prosper trial: Chemotherapy-related endpoints in patients with nonmetastatic castration-resistant prostate cancer treated with enzalutamide                                                                            | Journal of Urology           | 2018 | 199     | 4      | e231-e231 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                      | Título                                                                                                                                                                                                                                                                                                       | Revista                         | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| D and Krivoschik, A and Sternberg, C N                                                                                                                                     |                                                                                                                                                                                                                                                                                                              |                                 |      |         |        |             |                                |
| Morris, M J and Lorient, Y and Sweeney, C and Fizazi, K and Ryan, C J and Shevrin, D H and Antonarakis, E S and Reeves, J and Chandrawansa, K and Kornacker, M and al., et | Updated results: a phase I/IIa randomized trial of radium-223 + docetaxel versus docetaxel in patients with castration-resistant prostate cancer and bone metastases                                                                                                                                         | Journal of clinical oncology    | 2016 | 34      |        |             | Tipo de publicación equivocada |
| Conteduca, V and Brighi, N and Gurioli, G and Wetterskog, D and Giunta, E F and Lolli, C and Schepisi, G and Chiuri, V E and Gasparro, D and Zucali, P A and al., et       | LBA71 Open-label, multicentre randomised trial of Radium223-docetaxel versus docetaxel-Radium223 sequence in metastatic castration resistant prostate cancer (mCRPC) with prospective biomarker evaluation (RAPSON study)                                                                                    | Annals of oncology              | 2024 | 35      |        | S1259-S1259 | Tipo de publicación equivocada |
| Armstrong, A J and Szmulewitz, R Z and Petrylak, D and Villers, A and Azad, A and Alcaraz, A and Alekseev, B and Iguchi, T and Shore, N D and Rosbrook, B and al., et      | Phase 3 study of androgen deprivation therapy with enzalutamide or placebo in metastatic hormone-sensitive prostate cancer: the ARCHES trial                                                                                                                                                                 | Urology annals                  | 2020 | 12      |        | S30-S30     | Tipo de publicación equivocada |
| Merseburger, A S and Attard, G and Boysen, G and Gourgioti, G and Martins, K and Chowdhury, S                                                                              | A randomized, double-blind, placebo (PBO)-controlled, phase 3b study of the efficacy and safety of continuing enzalutamide (ENZA) in chemotherapy-naïve, metastatic castration-resistant prostate cancer (mCRPC) patients (pts) treated with docetaxel (DOC) plus prednisolone (PDN) who have progressed ... |                                 | 2022 | 40      | 6      |             | Tipo de publicación equivocada |
| Wedel, S A and Mellado, B and Sartor, O and Vogelzang, N and Hoskin, P and Nilsson, S and Coleman, R and Parker, C and Wahba, M and Haugen, I and al., et                  | Further characterization of the effects on sequential treatment of docetaxel before or after radium-223 dichloride therapy in Castration-Resistant Prostate Cancer (CRPC) patients with symptomatic bone metastases included in the phase 3 ALSYMPCA trial                                                   | Oncology research and treatment | 2015 | 38      |        | 267-267     | Tipo de publicación equivocada |
| Tombal, B F and Castellano, D and Kramer, G and Eymard, J-C and De Bono, J S and Sternberg, C N and Fizazi, K and Wulfing, C and Bamias, A and Carles, J and al., et       | CARD: overall survival (OS) analysis of patients with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel versus abiraterone or enzalutamide                                                                                                                                       | Journal of clinical oncology    | 2020 | 38      | 15     |             | Tipo de publicación equivocada |
| Clarke, N and Wiechno, P J and Alekseev, B and Sala, N and Jones, R and Kocak, I and                                                                                       | Olaparib combined with abiraterone in patients (pts) with metastatic                                                                                                                                                                                                                                         | Journal of Clinical Oncology    | 2018 | 36      | 15     |             | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                         | Título                                                                                                                                                                                                            | Revista                      | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Chiuri, V E and Jassem, J and Flechon, A and Redfern, C and Goessl, C D and Burgents, J and Kozarski, R and Hodgson, D R and Saad, F                                                          | castrationresistant prostate cancer (mCRPC): A randomized phase II trial                                                                                                                                          |                              |      |         |        |           |                                |
| Vogelzang, N J and Helle, S I and Johannessen, D C and O'Sullivan, J M and Garcia-Vargas, J E and O'Bryan-Tear, C G and Shan, M and Parker, C                                                 | Efficacy and safety of radium-223 dichloride (Ra-223) in castration-resistant prostate cancer (CRPC) patients with bone metastases who did or did not receive prior docetaxel (D) in the phase III ALSYMPCA trial | Journal of clinical oncology | 2013 | 31      | 15     |           | Tipo de publicación equivocada |
| Miller, K and Sartor, A O and Heinrich, D and Helle, S I and O'Sullivan, J M and Fossa, S D and Chodacki, A and Demkow, T and Logue, J P and Seke, M and al., et                              | Radium-223 chloride impact on skeletal-related events in patients with castration-resistant prostate cancer (CRPC) with bone metastases: a phase III randomized trial (ALSYMPCA)                                  | Onkologie                    | 2012 | 35      |        | 238-239   | Tipo de publicación equivocada |
| Stenzl, A and Szmulewitz, R Z and Petrylak, D and Holzbeierlein, J and Villers, A and Azad, A and Alcaraz, A and Alekseev, B and Iguchi, T and Shore, N D and al., et                         | Arches - Efficacy of androgen deprivation therapy with enzalutamide or placebo in metastatic hormone-sensitive prostate cancer: prostate-specific antigen results                                                 | Journal of urology           | 2019 | 201     | 4      | e996-e996 | Tipo de publicación equivocada |
| Parker, C and Nilsson, S and Heinrich, D and O'Sullivan, J M and Fossa, S D and Chodacki, A and Wiechno, P J and Logue, J P and Seke, M and Widmark, A and al., et                            | Updated analysis of the phase III, double-blind, randomized, multinational study of radium-223 chloride in castration-resistant prostate cancer (CRPC) patients with bone metastases (ALSYMPCA)                   | Journal of clinical oncology | 2012 | 30      | 18     |           | Tipo de publicación equivocada |
| Llacer Perez, C and Romero Laorden, N and Lozano Meiorada, R and Piulats, J M and Puente, J and Lorente Estelles, D and Medina, A and Cattrini, C and Vitrone, F M and Almagro, E and al., et | Treatment in CARD eligible metastatic castration resistant prostate cancer (mCRPC) patients according to the status of germline HRR mutations: cabazitaxel (CBZ) vs enzalutamide/abiraterone                      | Annals of oncology           | 2020 | 31      |        | S518-S519 | Tipo de publicación equivocada |
| Shore, N D and Moul, J W and Crawford, E and Van Der Meulen, E and Olesen, T and Persson, B                                                                                                   | Prostate-specific antigen (PSA) progression-free survival (PFS): a comparison of degarelix versus leuprolide in patients with prostate cancer                                                                     | Journal of clinical oncology | 2011 | 29      | 7      |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                | Título                                                                                                                                                                                                                                     | Revista                                   | Año  | Volumen | Número | Páginas    | Razón de exclusión             |
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| Caffo, O and Armstrong, A J and Szmulewitz, R and Petrylak, D and Villers, A and Azad, A and Alcaraz, A and Alekseev, B and Iguchi, T and Shore, N D and al., et     | Phase 3 study of androgen deprivation therapy (ADT) with enzalutamide (ENZA) or placebo (PBO) in metastatic hormone-sensitive prostate cancer (MHSPC): the ARCHES trial                                                                    | Tumori                                    | 2019 | 105     | 6      | 117-118    | Tipo de publicación equivocada |
| Sartor, O and Coleman, R and Nilsson, S and Heinrich, D and Staudacher, K and Garcia-Vargas, J and Vogelzang, N                                                      | Radium-223(R a-223) safety and efficacy in prostate cancer with bone metastases: phase 3 ALSYMPCA study findings stratified by age                                                                                                         | BJU international                         | 2013 | 112     |        | 15-16      | Tipo de publicación equivocada |
| Nilsson, S and Vogelzang, N J and Sartor, A O and Bottomley, D and Coleman, R E and Skjorestad, I and Wahba, M and Parker, C                                         | 1.5-year post-treatment follow-up of radium-223 dichloride (Ra-223) in patients with castration-resistant prostate cancer (CRPC) and bone metastases from the phase 3 ALSYMPCA study                                                       | Journal of clinical oncology              | 2014 | 32      | 4      |            | Tipo de publicación equivocada |
| Hofman, M and Emmett, L and Sandhu, S and Iravani, A and Joshua, A and Goh, J and Pattison, D and Tan, H and Kirkwood, I and Ng, S and al., et                       | TheraP: a randomised phase 2 trial of 177Lu-PSMA-617 (LuPSMA) theranostic versus cabazitaxel in metastatic castration resistant prostate cancer (mCRPC) progressing after docetaxel-initial results (ANZUP protocol 1603)                  | Asia-Pacific journal of clinical oncology | 2020 | 16      |        | 56-56      | Tipo de publicación equivocada |
| Clarke, N W and Thierry-Vuillemin, A and Wiechno, P J and Alekseev, B and Sala, N and Jones, R and Kocak, I and Chiuri, V E and Jassem, J and Flechon, A and al., et | Health-related quality of life (HRQoL) in patients with metastatic castration-resistant prostate cancer (mCRPC) treated with olaparib in combination with abiraterone                                                                      | Journal of clinical oncology              | 2019 | 37      |        |            | Tipo de publicación equivocada |
| De Wit, R and Kramer, G and Eymard, J-C and De Bono, J S and Sternberg, C N and Fizazi, K and Tombal, B and Wulfing, C and Bamias, A and Carles, J and al., et       | CARD: randomized, open-label study of cabazitaxel (CBZ) vs abiraterone (ABI) or enzalutamide (ENZ) in metastatic castration-resistant prostate cancer (mCRPC)                                                                              | Annals of oncology                        | 2019 | 30      |        | v882-v883  | Tipo de publicación equivocada |
| Parker, C and Heinrich, D and Helle, S I and O'Sullivan, J M and Fossa, S and Chodacki, A and Demkow, T and Logue, J and Seke, M and Widmark, A and al., et          | Overall survival benefit and impact on skeletal-related events for radium-223 chloride (Alpharadin) in the treatment of castration-resistant prostate cancer (CRPC) patients with bone metastases: a phase III randomized trial (ALSYMPCA) | European urology, supplements             | 2012 | 11      | 1      | e130-e130a | Tipo de publicación equivocada |
| Wei, J and Dong, R and Liu, F and Wang, S and Liu, Y and Cheng, F                                                                                                    | Therapeutic Effects of Abiraterone vs. Docetaxel on Castration-Resistant Prostate Cancer                                                                                                                                                   | Anti-tumor pharmacy                       | 2019 | 9       | 3      | 414-417    | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                                                                        | Título                                                                                                                                                                                                                                                          | Revista                       | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
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| Armstrong, A J and Szmulewitz, R Z and Petrylak, D P and Holzbeierlein, J M and Villers, A and Azad, A and Alcaraz, A and Alekseev, B Y and Iguchi, T and Shore, N D and al., et                                                             | ARCHES: efficacy of androgen deprivation therapy (ADT) with enzalutamide (ENZA) or placebo (PBO) in metastatic hormone-sensitive prostate cancer (mHSPC)                                                                                                        | Journal of clinical oncology  | 2019 | 37      |        |                 | Tipo de publicación equivocada |
| Heinrich, D and Helle, S I and Chodacki, A and Wiechno, P and Garcia-Vargas, J and Staudacher, K and Parker, C                                                                                                                               | Updated analysis of radium-223 dichloride (Ra-223) impact on pain, skeletal-related events (SRE), and survival from the phase 3 randomized trial (ALSYMPCA) in patients with castration-resistant prostate cancer (CRPC) and bone metastases                    | European urology, supplements | 2013 | 12      | 1      | e101-e102       | Tipo de publicación equivocada |
| Saad, F and Evans, C and Higano, C and Keane, T and Andriole, G and Iversen, P and Miller, K and Kim, C and Kimura, G and Armstrong, A and al., et                                                                                           | The prevail study: primary and non-visceral/visceral disease subgroup results for enzalutamide-treated men with metastatic castration-resistant prostate cancer                                                                                                 | Urology                       | 2014 | 84      | 4      | S98-S99         | Tipo de publicación equivocada |
| Smith, M R and Parker, C C and Saad, F and Miller, K and Tombal, B and Ng, Q S and Bogemann, M and Matveev, V and Piulats, J M and Zucca, L E and al., et                                                                                    | ERA 223: a phase III trial of radium-223 (Ra-223) in combination with abiraterone acetate and prednisone/prednisolone for the treatment of asymptomatic or mildly symptomatic chemotherapy-naïve patients (PTS) with bone-predominant metastatic castration-res | Annals of oncology            | 2018 | 29      |        | viii723-viii723 | Tipo de publicación equivocada |
| Kessel, A and McFarland, T R and Sayegh, N and Morton, K and Sirohi, D and Kohli, M and Swami, U and Nussenzweig, R and Agarwal, N and Maughan, B L                                                                                          | Randomized phase II trial of radium-223 (RA) plus enzalutamide (EZ) versus EZ alone in metastatic castrationrefractory prostate cancer (mCRPC): final efficacy and safety results                                                                               | Journal of clinical oncology  | 2021 | 39      | 6      |                 | Tipo de publicación equivocada |
| Armstrong, A J and Iguchi, T and Azad, A A and Szmulewitz, R Z and Holzbeierlein, J and Villers, A and Alcaraz, A and Alekseev, B Y and Shore, N D and Petrylak, D P and Rosbrook, B and Zohren, F and Yamada, S and Haas, G P and Stenzl, A | LBA25 Final overall survival (OS) analysis from ARCHES: A phase III, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) + androgen deprivation therapy (ADT) in men with metastatic hormone-sensitive prostate cancer (mHSPC)      | Annals of Oncology            | 2021 | 32      |        | S1300-S1301     | Tipo de publicación equivocada |

| Autor                                                                                                                                                                            | Título                                                                                                                                                                                                                                            | Revista                                                    | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Kuczyk, M A and Parker, C and Heinrich, D and O'Sullivan, J M and Fossa, S D and Chodacki, A and Demkow, T and Logue, J P and Seke, M and Widmark, A and al., et                 | Overall survival benefit and safety profile of radium-223 chloride, a first-in-class alpha-pharmaceutical: results from a phase III randomized trial (ALSYMPCA) in patients with castration-resistant prostate cancer (CRPC) with bone metastases | Onkologie                                                  | 2012 | 35      |        | 182-182     | Tipo de publicación equivocada |
| Sartor, O and Heinrich, D and Helle, S I and O'Sullivan, J M and Chodacki, A and Demkow, T and Logue, J and Seke, M and Widmark, A and Johannessen, D C and al., et              | Radium-223 chloride (alpharadin) impact on overall survival and skeletal-related events in patients with castration-resistant prostate cancer with bone metastases: a phase III randomized trial (ALSYMPCA)                                       | Journal of urology                                         | 2012 | 187     | 4      | e279-e279   | Tipo de publicación equivocada |
| Oliver Sartor, A and Heinrich, D and O'Sullivan, J M and Fossa, S D and Chodacki, A and Wiechno, P J and Logue, J P and Seke, M and Widmark, A and Johannessen, D C and al., et  | Radium-223 chloride (Ra-223) impact on skeletal-related events (SREs) and ECOG performance status (PS) in patients with castration-resistant prostate cancer (CRPC) with bone metastases: interim results of a phase III trial (ALSYMPCA)         | Journal of clinical oncology                               | 2012 | 30      | 15     |             | Tipo de publicación equivocada |
| Petrylak, D P and Vaishampayan, U N and Patel, K R and Higano, C S and Albany, C and Dawson, N A and Mehlhaff, B A and Quinn, D I and Nordquist, L T and Wagner, V J and al., et | A phase IIa study of radium-223 dichloride (Ra-223) alone or in combination with abiraterone acetate or enzalutamide in metastatic castration-resistant prostate cancer (mCRPC)                                                                   | Annals of oncology                                         | 2019 | 30      |        | v340-v341   | Tipo de publicación equivocada |
| O'Sullivan, J M and Parker, C and Cross, A and O'Bryan-Tear, C G and Garcia-Vargas, J and Sartor, O                                                                              | Results from a phase III randomized trial (ALSYMPCA) of radium-223 chloride, a first-in-class alpha-emitter, in patients with castration-resistant prostate cancer (CRPC) and bone metastases: overall survival benefit and safety profile        | European journal of nuclear medicine and molecular imaging | 2012 | 39      |        | S294-S294   | Tipo de publicación equivocada |
| McKay, R R and Xie, W and Lis, R and Ye, H and Zhang, Z and Trinh, Q-D and Chang, S L and Harshman, L C and                                                                      | Results of a phase II trial of neoadjuvant abiraterone + prednisone+ enzalutamide + leuprolide (APEL) versus enzalutamide + leuprolide (EL) for patients with high-risk                                                                           | Journal of clinical oncology                               | 2018 | 36      | 6      |             | Tipo de publicación equivocada |

| Autor                                                                                                                                                                | Título                                                                                                                                                                                                                                                          | Revista                                                    | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Parker, C and Heinrich, D and O'Sullivan, J M and Fossa <sup>o</sup> , S and Chodacki, A and Demkow, T and Cross, A and Bolstad, B and Garcia- OVargas, J and Sartor | Overall survival benefit of radium-223 chloride (Alpharadin™) in the treatment of patients with symptomatic bone metastases in Castration-resistant Prostate Cancer (CRPC): a phase III randomized trial (ALSYMPCA)                                             | European journal of cancer                                 | 2011 | 47      |        | 3-3       | Tipo de publicación equivocada |
| Fizazi, K and Kramer, G and Eymard, J-C and De Bono, J S and Sternberg, C N and Tombal, B F and Castellano, D and Wulfing, C and Lontos, M and Carles, J and al., et | Pain response and health-related quality of life (HRQL) analysis in patients with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel (CBZ) versus abiraterone or enzalutamide in the CARD study                                      | Journal of clinical oncology                               | 2020 | 38      | 6      |           | Tipo de publicación equivocada |
| Wedel, S and Kranert, T W and Chodacki, A and Staudacher, K and Garcia-Vargas, J and Parker, C                                                                       | Updated analysis of radium-223 dichloride (Ra-223) impact on survival, safety, and skeletal-related events in castration-resistant prostate cancer (CRPC) patients with bone metastases from the phase 3 ALSYMPCA trial                                         | European journal of nuclear medicine and molecular imaging | 2013 | 40      |        | S190-S190 | Tipo de publicación equivocada |
| Sweeney, C and Martin, A J and Zielinski, R R and Thomson, A and Tan, T H and Sandhu, S K and Reaume, M N and Pook, D W and Parnis, F and North, S A and al., et     | Overall survival (OS) results of a phase III randomized trial of standard-of-care therapy with or without enzalutamide for metastatic hormone-sensitive prostate cancer (mHSPC): ENZAMET (ANZUP 1304), an ANZUP-led international cooperative group trial       | Journal of clinical oncology                               | 2019 | 37      |        |           | Tipo de publicación equivocada |
| Chowdhury, S and Davidson, R and Coppell, A and Mobasher, H and Stari, A and Snijder, R and Treadwell, C and Merseburger, A S                                        | The PRESIDE trial: A randomized, double-blind, placebo-controlled phase III efficacy and safety study of continued enzalutamide plus docetaxel after disease progression on enzalutamide alone in patients with metastatic castration-resistant prostate cancer | Journal of Clinical Oncology                               | 2015 | 33      | 15     |           | Tipo de publicación equivocada |
| Shore, N and Sartor, O and Vogelzang, N and Hoskin, P and Nilsson, S and Coleman, R and Parker, C and Wahba, M and Staudacher, K                                     | Further characterization of the effects of prior or no prior docetaxel therapy on CRPC patients with bone metastases receiving Ra-223 in the phase 3 alsympca trial                                                                                             | Journal of urology                                         | 2014 | 191     | 4      | e810-e810 | Tipo de publicación equivocada |
| Armstrong, A J and Iguchi, T and Azad, A and Szmulewitz, R Z and Holzbeierlein, J and Villers, A and Alcaraz, A and Alexeev, B and Shore, N D                        | Overall survival (OS) in patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC) treated with enzalutamide (ENZA) + androgen deprivation therapy (ADT) by                                                                                      | Journal of clinical oncology                               | 2022 | 40      | 6      |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                     | Título                                                                                                                                                                                                                                                         | Revista                      | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| and Gomez-Veiga, F and al., et                                                                                                                                            | high or low disease volume and progression to mHSPC (M0 at diagnosis) or de novo mHS                                                                                                                                                                           |                              |      |         |        |             |                                |
| Ye, D and Zou, Q and Sun, Z and Sun, Y and Li, C and Du, C and Chen, Z and Shan, Y and Huang, Y and Jin, J and al., et                                                    | Abiraterone acetate after docetaxel-based chemotherapy failure in Asian patients with metastatic castration-resistant prostate cancer                                                                                                                          | BJU international            | 2015 | 116     |        | 9-9         | Tipo de publicación equivocada |
| Shore, N and Heidenreich, A and Villers, A and Klotz, L and Hussain, M and Karsh, L and Van Os, S and Baron, B and Wang, F and Forer, D and al., et                       | Terrain trial: prostate-specific antigen kinetics and quality of life results of enzalutamide versus bicalutamide in metastatic castration-resistant prostate cancer                                                                                           | Journal of urology           | 2015 | 193     | 4      | e411-e411   | Tipo de publicación equivocada |
| Armstrong, A J and Tombal, B and Sternberg, C N and Higano, C S and Rathkopf, D E and Lortot, Y and Saad, F and Joshua, A M and De Bono, J S and Venner, P M and al., et  | Primary, secondary, and quality-of-life endpoint results from PREVAIL, a phase 3 study of enzalutamide in men with metastatic castration resistant prostate cancer (mCRPC)                                                                                     | Journal of clinical oncology | 2014 | 32      | 15     |             | Tipo de publicación equivocada |
| Petrylak, D P and Azad, A A and Szmulewitz, R Z and Iguchi, T and Shore, N D and Holzbeierlein, J and Alekseev, B and El-Chaar, N N and Rosbrook, B and Ma, J and al., et | 1398P Overall survival (OS) in patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC) who received prior androgen deprivation therapy (ADT) and reached low prostate-specific antigen (PSA) levels treated further with enzalutamide (ENZA): | Annals of oncology           | 2022 | 33      |        | S1183-S1184 | Tipo de publicación equivocada |
| Smith, M R and Hussain, M H A and Saad, F and Fizazi, K and Sternberg, C N and Crawford, E D and Kopylov, E and Park, C H and Alexeev, B and Montes, A and al., et        | Overall survival with darolutamide versus placebo in combination with androgen-deprivation therapy and docetaxel for metastatic hormone-sensitive prostate cancer in the phase 3 ARASENS trial                                                                 | Journal of clinical oncology | 2022 | 40      | 6      |             | Tipo de publicación equivocada |
| Sternberg, C N and Castellano, D and De Bono, J S and Fizazi, K and Tombal, B F and Wulfing, C and Kramer, G and Eymard, J-C and Bamias, A and Carles, J and al., et      | Efficacy and safety in older patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) receiving cabazitaxel (CBZ) versus abiraterone (ABI) or enzalutamide (ENZ) in the CARD study                                                          | Journal of clinical oncology | 2020 | 38      | 15     |             | Tipo de publicación equivocada |
| Kramer, G and Sternberg, C N and Fizazi, K and Tombal, B and Eymard, J-C and De                                                                                           | Effect of cabazitaxel vs abiraterone or enzalutamide on patient-reported outcomes in metastatic castration-resistant prostate                                                                                                                                  | Journal of urology           | 2020 | 203     |        | e366-e366   | Tipo de publicación equivocada |



| Autor                                                                                                                                                                                                                                                                                                                                           | Título                                                                                                                                                                                                                                                  | Revista                       | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Rush, H L and Cook, A D and Brawley, C D and Murphy, L and MacNair, A and Millman, R and Attard, G and Clarke, N and Morgans, A K and Chowdhury, S and al., et                                                                                                                                                                                  | Comparative quality of life in patients randomized contemporaneously to docetaxel or abiraterone in the STAMPEDE trial                                                                                                                                  | Journal of clinical oncology  | 2020 | 38      | 6      |           | Tipo de publicación equivocada |
| Morris, M J and Gleave, M E and Armstrong, A J and Carducci, M A and Saad, F and Lacuna, K P and Scher, H I                                                                                                                                                                                                                                     | A randomized, open label, multicenter, phase 3, 2-arm study of androgen deprivation with leuprolide (L), ± docetaxel (D) for clinically asymptomatic prostate cancer (PC) subjects with a rising PSA following definitive local therapy: safety results | Journal of clinical oncology  | 2014 | 32      | 15     |           | Tipo de publicación equivocada |
| Shore, N D and Tombal, B and Hussain, M and Saad, F and Fizazi, K and Sternberg, C N and Crawford, E D and Nordquist, L and Tutrone, R and Belkoff, L and al., et                                                                                                                                                                               | EFFICACY AND SAFETY OF DAROLUTAMIDE IN COMBINATION WITH ANDROGEN-DEPRIVATION THERAPY AND DOCETAXEL IN THE NORTH AMERICAN POPULATION FROM ARASENS                                                                                                        | Journal of urology            | 2023 | 209     |        | e380-e380 | Tipo de publicación equivocada |
| Oudard, S and Sartor, O and Sengelov, L and Daugaard, G and Saad, F and Hansen, S and Hjelm-Eriksson, M and Jassem, J and Thiery-Vuillemin, A and Caffo, O and al., et                                                                                                                                                                          | FIRSTANA: health-related quality of life (HRQL) and post-hoc analyses for the phase III study assessing cabazitaxel (C) vs docetaxel (D) in chemotherapy-naïve patients (pts) with metastatic castration-resistant prostate cancer (mCRPC)              | Annals of oncology            | 2016 | 27      |        |           | Tipo de publicación equivocada |
| Tombal, B and Iversen, P and Miller, K and Tammela, T and Borre, M and Bjartell, A and Mulders, P and Kliment, J and Ramon, J and Matveev, V and Stenzl, A and Evans, C P and Sternberg, C N and Loriot, Y and De Bono, J and Carles, J and Kim, C S and Kimura, G and Noonberg, S and Bhattacharya, S and Perabo, F and Phung, D and Beer, T M | Enzalutamide in men with chemotherapy-naïve metastatic castration resistant prostate cancer (MCRPC): Primary and European regional results of the phase 3 prevail study                                                                                 | European Urology, Supplements | 2014 | 13      | 1      | LBA3-LBA3 | Tipo de publicación equivocada |

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| Sartor, A O and Oudard, S and Sengelov, L and Daugaard, G and Saad, F and Hansen, S and Hjelm-Eriksson, M and Jassem, J and Thierry-Vuillemin, A and Caffo, O and al., et                                                                                                                        | Cabazitaxel vs docetaxel in chemotherapy-naïve (CN) patients with metastatic castration-resistant prostate cancer (mCRPC): a three-arm phase III study (FIRSTANA)                                                                                            | Journal of clinical oncology | 2016 | 34      |        |             | Tipo de publicación equivocada |
| Clarke, N W and Armstrong, A J and Thierry-Vuillemin, A and Oya, M and Shore, N and Procopio, G and Guedes, J D and Arslan, C and Mehra, N and Parnis, F and al., et                                                                                                                             | PROpel: efficacy of abiraterone + olaparib vs. abiraterone + placebo in the first-line treatment of patients with asymptomatic/mildly symptomatic metastatic castration-resistant prostate cancer (mCRPC) at baseline                                        | European urology             | 2023 | 83      |        | S1674-S1675 | Tipo de publicación equivocada |
| Chi, K N and Merseburger, A S and Ozguroglu, M and Chowdhury, S and Bjartell, A and Chung, B and Pereira De Santana Gomes, A J and Given, R and Juarez, A and Uemura, H and al., et                                                                                                              | The effect of prior docetaxel (DOC) treatment on efficacy and safety of apalutamide (APA) plus androgen deprivation therapy (ADT) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) from TITAN                                  | Journal of clinical oncology | 2022 | 40      | 6      |             | Tipo de publicación equivocada |
| Emmett, L and Subramaniam, S and Crumbaker, M and Joshua, A M and Weickhardt, A J and Lee, S T and Ng, S and Francis, R J and Goh, J C H and Pattison, D A and al., et                                                                                                                           | LBA84 Enzalutamide and 177Lu-PSMA-617 in poor-risk, metastatic, castration-resistant prostate cancer (mCRPC): a randomised, phase II trial: eNZA-p (ANZUP 1901)                                                                                              | Annals of oncology           | 2023 | 34      |        | S1325-S1325 | Tipo de publicación equivocada |
| Fizazi, K and Foulon, S and Carles, J and Roubaud, G and McDermott, R and Fléchon, A and Tombal, B and Supiot, S and Berthold, D and Ronchin, P and Kacso, G and Gravis, G and Calabro, F and JF, Berdah and Hasbini, A and Silva, M and Thierry-Vuillemin, A and Latorzeff, I and Mourey, L and | Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. PG - 1695-1707 LID |                              |      |         | 1474   |             | Tratamiento equivocado         |

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| Oudard, S and Latorzeff, I and Caty, A and Miglianico, L and Sevin, E and Hardy Bessard, A-C and Delva, R and Rolland, F and Chevreau, C and Priou, F and al., et                                                               | Docetaxel (D) with androgen suppression (AS) for high-risk localized prostate cancer (HrPC) patients (pts) who relapsed PSA after radical prostatectomy (RP) and/or radiotherapy (RT): a randomized phase III trial                                               | Annals of oncology           | 2017 | 28      |        | v269-v270 | Tipo de publicación equivocada |
| Hofman, M S and Emmett, L and Sandhu, S K and Iravani, A and Joshua, A M and Goh, J C and Pattison, D A and Tan, T H and Kirkwood, I D and Ng, S and al., et                                                                    | <sup>177</sup> Lu-PSMA-617 (LuPSMA) versus cabazitaxel in metastatic castration-resistant prostate cancer (mCRPC) progressing after docetaxel: updated results including progression-free survival (PFS) and patient-reported outcomes (PROs) (TheraP ANZUP 1603) | Journal of clinical oncology | 2021 | 39      | 6      |           | Tipo de publicación equivocada |
| Fleming, M T and Scher, H I and Fizazi, K and Taplin, M-E and Forer, D and Hirmand, M and De Bono, J S                                                                                                                          | Long-term responders to enzalutamide (ENZA) during the phase III AFFIRM trial: baseline characteristics and efficacy outcomes                                                                                                                                     | Journal of clinical oncology | 2013 | 31      | 6      |           | Tipo de publicación equivocada |
| Ye, D and Ahn, H and Pu, Y-S and Weiqing, H and Xie, L-P and Huang, S-P and Wu, H-C and Ma, L and Yamada, S and Noda, S and al., et                                                                                             | Efficacy and safety of enzalutamide (ENZ) vs placebo (PL) in chemotherapy-naïve patients (pts) with progressive metastatic castration-resistant prostate cancer (mCRPC) following androgen deprivation therapy (ADT): an Asian multinational study                | Annals of oncology           | 2016 | 27      |        |           | Tipo de publicación equivocada |
| Hussain, M and Mateo, J and Fizazi, K and Saad, F and Shore, N D and Sandhu, S and Chi, K N and Sartor, O and Agarwal, N and Olmos, D and al., et                                                                               | PRO found: phase III study of olaparib versus enzalutamide or abiraterone for metastatic castration-resistant prostate cancer (mCRPC) with homologous recombination repair (HRR) gene alterations                                                                 | Annals of oncology           | 2019 | 30      |        | v881-v882 | Tipo de publicación equivocada |
| Iguchi, T and Tamada, S and Kato, M and Yasuda, S and Otoshi, T and Machida, Y and Ohmachi, T and Ishii, K and                                                                                                                  | Impact of enzalutamide and sequential flutamide and enzalutamide therapy for castration-resistant prostate cancer after bicalutamide-combined androgen blockade therapy on overall survival: a follow-up study                                                    | Journal of clinical oncology | 2019 | 37      |        |           | Tipo de publicación equivocada |

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| Iwata, H and Yamamoto, S and al., et                                                                                                                                                                                                                                                                      | of randomized phase 2 trial (OCCU- CRPC study)                                                                                                                                                                                                            |                              |      |         |        |             |                                |
| Tombal, B and Hussain, M and Saad, F and Fizazi, K and Shore, N and Kopyltsov, E and Bogemann, M and Mendez-Vidal, M J and Littleton, N and Srinivasan, S and al., et                                                                                                                                     | Efficacy and safety of darolutamide in combination with androgen-deprivation therapy and docetaxel in European patients from the phase 3 ARASENS trial                                                                                                    | European urology             | 2024 | 85      |        | S1585-S1585 | Tipo de publicación equivocada |
| Hofman, M S and Emmett, L and Sandhu, S and Iravani, A and Joshua, A M and Goh, J C and Pattison, D A and Tan, T H and Kirkwood, I D and Francis, R J and al., et                                                                                                                                         | Thera P: 177Lu-PSMA-617 (LuPSMA) versus cabazitaxel in metastatic castrationresistant prostate cancer (mCRPC) progressing after docetaxel-Overall survival after median follow-up of 3 years (ANZUP 1603)                                                 | Journal of clinical oncology | 2022 | 40      | 16     |             | Tipo de publicación equivocada |
| de Bono, J S and Mateo, J and Fizazi, K and Saad, F and Shore, N and Sandhu, S and Chi, K N and Sartor, O and Agarwal, N and Olmos, D and Thiery-Vuillemin, A and Twardowski, P and Roubaud, G and Ozguroglu, M and Kang, J and Burgents, J and Gresty, C and Corcoran, C and Adelman, C A and Hussain, M | Final overall survival (OS) analysis of PROfound: Olaparib vs physician's choice of enzalutamide or abiraterone in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) and homologous recombination repair (HRR) gene alterations | Annals of Oncology           | 2020 | 31      |        | S508-S508   | Tipo de publicación equivocada |
| Ohlmann, C H and Stockle, M and Pfister, D and De Bono, J S and Molina, A and Frohn, C and Kheoh, T and Haqq, C M and Scher, H I and Wirth, M and al., et                                                                                                                                                 | Improved Overall Survival (OS) in patients with metastatic Castration Resistant Prostate Cancer (mCRPC) progressing after docetaxel-based chemotherapy: results from the phase III study COU-AA-301 with abiraterone acetate                              | Onkologie                    | 2011 | 34      |        | 9-10        | Tipo de publicación equivocada |
| Sydes, M R and Mason, M D and Spears, M R and Clarke, N W and Dearnaley, D and Ritchie, A W S and Russell, M and Gilson, C and Jones, R and De Bono, J and al., et                                                                                                                                        | PR Adding abiraterone acetate plus prednisolone (AAP) or docetaxel for patients (pts) with high-risk prostate cancer (PCa) starting long-term androgen deprivation therapy (ADT): directly randomised data from STAMPEDE (NCT00268476)                    | Annals of oncology           | 2017 | 28      |        | v619-v619   | Tipo de publicación equivocada |
| Saad, F and Armstrong, A J and Thiery-Vuillemin, A and Oya, M and Shore, N D and Procopio, G and Arslan, C and Mehra, N and Parnis, F and                                                                                                                                                                 | 13570 Biomarker analysis and updated results from the Phase III PROpel trial of abiraterone (abi) and olaparib (ola) vs abi and placebo (pbo) as first-line (1L) therapy                                                                                  | Annals of Oncology           | 2022 | 33      |        | S1160-S1160 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                    | Título                                                                                                                                                                                                                                                        | Revista                      | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Brown, E and Constans Schlurmann, F and Joung, J Y and Sugimoto, M and Sartor, O and Liu, Y.-Z. and Poehlein, C H and Desai, C and Del Rosario, P M D and Clarke, N      | for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC)                                                                                                                                                                               |                              |      |         |        |           |                                |
| Shore, N D and Clarke, N and Armstrong, A J and Oya, M and Procopio, G and Guedes, J D C and Arslan, C and Mehra, N and Brown, E and Schlurmann, F and al., et           | Efficacy of olaparib (O) plus abiraterone (A) versus placebo (P) plus A in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) with single homologous recombination repair gene mutations (HRRm) in the PROpel trial                  | Journal of clinical oncology | 2024 | 42      | 4      |           | Tipo de publicación equivocada |
| Stockler, M R and Martin, A J and Dhillon, H and Davis, I D and Chi, K N and Chowdhury, S and Horvath, L G and Lawrence, N J and Marx, G M and Mc Caffrey, J and al., et | Health-related quality of life (HRQL) in a randomized phase III trial of enzalutamide with standard first-line therapy for metastatic, hormone-sensitive prostate cancer (mHSPC): ENZAMET (ANZUP 1304), an ANZUP-led, international, co-operative group trial | Annals of oncology           | 2019 | 30      |        | v886-v887 | Tipo de publicación equivocada |
| Miller, K and Scher, H I and Fizazi, K and Basch, E M and Sternberg, C N and Hirmand, M and Cella, D and Ivanescu, C and Phung, D and Spalding, J R and al., et          | Effect of enzalutamide on health-related quality of life (HRQoL) in men with metastatic castration-resistant prostate cancer (mCRPC) following docetaxel-based therapy: results from the AFFIRM study                                                         | Journal of clinical oncology | 2013 | 31      | 6      |           | Tipo de publicación equivocada |
| Hofman, M and Emmett, L and Iravani, A and Sandhu, S and Joshua, A and Pattison, D and Goh, J and Kirkwood, I and Tan, T H and Francis, R and al., et                    | <sup>177</sup> Lu-PSMA-6i7 versus Cabazitaxel in Metastatic                                                                                                                                                                                                   | Journal of nuclear medicine  | 2021 | 62      |        |           | Tipo de publicación equivocada |
| Von Buren, M and Sternberg, N and Fizazi, K and Saad, F and Rathenborg, P and Shore, N D and Demirhan, E and Modelska, K and Phung, D and Krivoschik, A and al., et      | Prostate-specific antigen response with Enzalutamide in nonmetastatic castration-resistant prostate cancer: PROSPER                                                                                                                                           | Swiss medical weekly         | 2019 | 149     |        | 16S-17S   | Tipo de publicación equivocada |
| Fizazi, K and Scher, H I and Molina, A and Logothetis, C J and Jones, R J and Staffurth, J N and Li, J and Kheoh, T and Haqq, C M and De Bono, J S                       | Final overall survival (OS) analysis of COU-AA-301, a phase 3 study of abiraterone acetate plus prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) pretreated with docetaxel                                                 | European journal of cancer   | 2011 | 47      |        | S483-S484 | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                | Título                                                                                                                                                                                                                                                       | Revista                      | Año  | Volumen | Número | Páginas     | Razón de exclusión             |
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| Davis, I D and Martin, A J and Zielinski, R R and Thomson, A and Tan, T H and Sandhu, S and Reaume, M N and Pook, D W and Parnis, F and North, S A and al., et                       | Updated overall survival outcomes in ENZAMET (ANZUP 1304), an international, cooperative group trial of enzalutamide in metastatic hormone-sensitive prostate cancer (mHSPC)                                                                                 | Journal of clinical oncology | 2022 | 40      | 17     |             | Tipo de publicación equivocada |
| Caffo, O and Palesandro, E and Nole, F and Gasparro, D and Mucciarini, C and Aieta, M and Zagonel, V and Iacovelli, R and De Giorgi, U F F and Rossetti, S and al., et               | Updated survival analyses of a multicentric phase II randomized trial of docetaxel (D) plus enzalutamide (E) versus docetaxel (D) as first-line chemotherapy for patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) (CHEIRON study) | Annals of oncology           | 2019 | 30      |        | v333-v333   | Tipo de publicación equivocada |
| Wang, S and Fu, C and Li, Y and Xing, J and Zhou, L and Yang, Y and Wang, H and Smith, M R and Tombal, B and Hussain, M and al., et                                                  | Darolutamide (DARO) in combination with androgen-deprivation therapy (ADT) and docetaxel (DOC) in Chinese patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC) in the phase III ARASENS study                                            | Annals of oncology           | 2023 | 34      |        | S1572-S1572 | Tipo de publicación equivocada |
| Selvaggi, F P and Battaglia, M and Disabato, G and Del Monaco, D and Lunglmayr, G and Boccardo, F and Calabria, C and Martorana, G and Oneto, F and Ziveri, M and al., et            | Goserelin depot versus Goserelin depot plus flutamide in the treatment of advanced prostate carcinoma. Results of a randomized international multicentric study                                                                                              | Acta urologica italica       | 1992 | 6       |        | 303-307     | No se encuentra texto completo |
| Iguchi, T and Tamada, S and Kato, M and Yasuda, S and Machida, Y and Ohmachi, T and Ishii, K and Iwata, H and Yamamoto, S and Kanamaru, T and al., et                                | Enzalutamide versus flutamide for castration-resistant prostate cancer after combined androgen blockade therapy with bicalutamide: a multicenter randomized phase II trial (OCUU-CRPC study)                                                                 | Journal of clinical oncology | 2019 | 37      |        |             | No se encuentra texto completo |
| Petrylak, D P and Fizazi, K and Sternberg, C N and Budnik, N and De Wit, R and J. Wiechno, P and Bellmunt, J and Barton, D and Fandi, A and Jungnelius, U and Li, S and Vogelzang, N | A phase 3 study to evaluate the efficacy and safety of docetaxel and prednisone (DP) with or without lenalidomide (LEN) in patients with castrate-resistant prostate cancer (CRPC): The mainsail trial                                                       | Annals of Oncology           | 2012 | 23      |        | ix15-ix15   | Tipo de publicación equivocada |
| Oudard, S M and Bevans, K B and Attard, G and Efstathiou, E and Flaig, T W and Franke, F A and Goodman, O B and De                                                                   | Health-related quality of life (HRQoL) in ACIS: a phase III trial of apalutamide with abiraterone acetate and prednisone (APA +                                                                                                                              | Annals of oncology           | 2021 | 32      |        | S634-S634   | Tipo de publicación equivocada |

| Autor                                                                                                                                                                                     | Título                                                                                                                                                                                                                                                          | Revista                         | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
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| Giorgi, U and Pieczonka, C M and Yeruva, K and al., et                                                                                                                                    | AAP) vs AAP in metastatic castration-resistant prostate cancer (mCRPC)                                                                                                                                                                                          |                                 |      |         |        |           |                                |
| Duran, I and Grande, E and Castellano, D E and Font, A and Saez, M I and Puente, J and Santander, C and Mendez-Vidal, M J and Arika, J A A and Mellado, B and al., et                     | Randomized phase II study of abiraterone acetate (AA) maintenance in combination with docetaxel after disease progression to AA in metastatic castration resistant prostate cancer (mCRPC): preliminary safety results of first line AA treatment-ABIDO-SOGUG T | Journal of clinical oncology    | 2015 | 33      | 15     |           | Tipo de publicación equivocada |
| Haefliger, J-M                                                                                                                                                                            | Randomized study comparison Zoladex with a combination of Zoladex plus flutamide in the treatment of advanced prostate cancer                                                                                                                                   | Helvetica chirurgica acta       | 1992 | 59      | 3      | 477-483   | No se encuentra texto completo |
| Sternberg, C N and Fizazi, K and Saad, F and Rathenborg, P and Shore, N and Demirhan, E and Modelska, K and Phung, D and Krivoshik, A and Hussain, M                                      | Prostate-specific antigen (PSA) response in men with nonmetastatic castration-resistant prostate cancer (M0 CRPC) treated with enzalutamide (ENZA): Results from PROSPER                                                                                        | European Urology, Supplements   | 2018 | 17      | 2      | e868-e869 | Tipo de publicación equivocada |
| Iguchi, T and Kato, M and Tamada, S and Yasuda, S and Machida, Y and Ohmachi, T and Ishii, K and Iwata, H and Yamamoto, S and Kanamaru, T and al., et                                     | Relevance of alternative anti-androgen therapy for castration-resistant prostate cancer after combined androgen blockade: a prospective observational study of OCCU-CRPC cohort                                                                                 | Journal of urology              | 2021 | 206     |        | e60-e61   | Diseño de estudio equivocado   |
| Saad, F and Shore, N and Feyerabend, S and Pieczonka, C and Vogelzang, N and Lacombe, L and Tanguay, S and Uemura, H and Lee, J Y and Wu, W-J and al., et                                 | Efficacy of physician's choice of enzalutamide or abiraterone in the control arm of profound                                                                                                                                                                    | Journal of urology              | 2021 | 206     |        | e586-e586 | Tipo de publicación equivocada |
| Merseburger, A S and Chowdhury, S and Agarwal, N and Bjartell, A and Chung, B H and Pereira de Santana Gomes, A J and Given, R W and Soto, A J and Ozguroglu, M and Uemura, H and al., et | TITAN, a phase 3 study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate cancer (mCSPC) receiving androgen deprivation therapy (ADT)                                                                    | Oncology research and treatment | 2019 | 42      |        | 286-286   | Tipo de publicación equivocada |
| Chi, K N and Agarwal, N and Bjartell, A and Chung, B H and De Santana Gomes, A J P and Given, R W and Soto, A J and Merseburger, A S and                                                  | First results from TITAN: a phase III double-blind, randomized study of apalutamide (APA) versus placebo (PBO) in patients (pts) with metastatic castration-sensitive prostate                                                                                  | Journal of clinical oncology    | 2019 | 37      |        |           | Tipo de publicación equivocada |

| Autor                                                                                                                                                                        | Título                                                                                                                                                                                                         | Revista                                          | Año  | Volumen | Número | Páginas         | Razón de exclusión             |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|------|---------|--------|-----------------|--------------------------------|
| Ozguroglu, M and Uemura, H and al., et                                                                                                                                       | cancer (mCSPC) receiving androgen deprivation therapy (ADT)                                                                                                                                                    |                                                  |      |         |        |                 |                                |
| Miller, K and Scher, H and Fizazi, K and Basch, E and Sternberg, C and Hirmand, M and Cella, D and Ivanescu, C and Phung, D and Spalding, J and al., et                      | Enzalutamide improves health-related quality of life in men with metastatic castration-resistant prostate cancer following docetaxel-based therapy: results from the affirm study                              | Urology                                          | 2013 | 82      | 3      | S52-S52         | Diseño de estudio equivocado   |
| Park, H S and Shin, S H and Woo, S H and Jeon, S H and Kang, S H and Shin, D W and Park, J                                                                                   | Quality of life in prostate cancer patients treated with primary androgen deprivation therapy: comparison of combined androgen blockade vs. LHRH agonist alone                                                 | Journal of urology                               | 2019 | 201     | 4      | e469-e470       | Tipo de publicación equivocada |
| De Bono, J S and Fizazi, K and Saad, F and Shore, N D and Roubaud, G and Ozguroglu, M and Penel, N and Matsubara, N and Mehra, N and Procopio, G and al., et                 | PROfound: efficacy of olaparib (ola) by prior taxane use in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC) and homologous recombination repair (HRR) gene alterations             | Journal of clinical oncology                     | 2020 | 38      | 6      |                 | Tipo de publicación equivocada |
| Sternberg, C N and Fizazi, K and Saad, F and Shore, N D and De Giorgi, U and Penson, D F and Ferreira, U and Ivashchenko, P and Efsthathiou, E and Madziarska, K and al., et | Final overall survival (OS) from PROSPER: a phase III, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (nmCRPC) | Journal of clinical oncology                     | 2020 | 38      | 15     |                 | Tipo de publicación equivocada |
| Strolin, P and Cislo, P and Sartor, O and Reuning-Scherer, J and Shan, M and Zhan, L and Parker, C                                                                           | Effects of radium-223 dichloride (Ra-223) on health-related quality of life (HRQoL) assessed by the EQ-5D utility scores in ALSYMPCA                                                                           | Oncology research and treatment                  | 2015 | 38      |        | 82-82           | Tipo de publicación equivocada |
| Altwein, J E and Klippel, K F and Holdaway, I and Lungmayr, G and Tyrrell, C J and Varenhorst, E                                                                             | A multicenter randomized trial comparing the LHRH agonist zoladex in combination with flutamide in the treatment of advanced prostate cancer                                                                   | Journal of cancer research and clinical oncology | 1990 | 116     |        | 548-548         | Tipo de publicación equivocada |
| Hoyle, A P and Ali, S A and James, N D and Parker, C C and Cook, A D and Attard, G and Chowdhury, S and Cross, W and Dearnaley, D P and De Bono, J S and al., et             | Effects of abiraterone acetate plus prednisone/prednisolone in high and low risk metastatic hormone sensitive prostate cancer                                                                                  | Annals of oncology                               | 2018 | 29      |        | viii722-viii722 | Tipo de publicación equivocada |
| Goodman, O B and Flaig, T W and Molina, A and Mulders, P and Suttman, H and Li, J and                                                                                        | Exploratory analysis of the visceral disease (VD) patient subset in COU-AA-301, a phase III study of abiraterone acetate (AA) in                                                                               | Journal of clinical oncology                     | 2013 | 31      | 6      |                 | Tipo de publicación equivocada |



| Autor                                                                                                                                                         | Título                                                                                                                                                                                                                                                                                                       | Revista                                   | Año  | Volumen | Número | Páginas   | Razón de exclusión             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|------|---------|--------|-----------|--------------------------------|
| Kheoh, T S and De Bono, J S and Scher, H I                                                                                                                    | metastatic castration-resistant prostate cancer (mCRPC)                                                                                                                                                                                                                                                      |                                           |      |         |        |           |                                |
| Saad, F and De Bono, J S and Haqq, C M and Logothetis, C J and Fizazi, K and Jones, R J and Chi, K N and Kheoh, T and Scher, H I and Molina, A                | Abiraterone acetate plus low-dose prednisone has a favorable safety profile, improves survival and produces PSA and radiographic responses in metastatic castration-resistant prostate cancer progressing after docetaxel-based chemotherapy: Results from COU-AA-301, a randomized, double-blind, placeb... | J. Urol.                                  | 2011 | 185     | 4      | e283-e284 | Tipo de publicación equivocada |
| Tombal, B and Hussain, M and Fizazi, K and Saad, F and Rathenborg, P and Shore, N D and Demirhan, E and Modelska, K and Phung, D and Krivoshik, A and al., et | PROSPER: a phase 3 study of enzalutamide (ENZA) in men with non-metastatic castration-resistant prostate cancer (nmCRPC)                                                                                                                                                                                     | Swiss medical weekly                      | 2018 | 148     |        | 15S-15S   | Tipo de publicación equivocada |
| Hussain, M and Fizazi, K and Saad, F and Rathenborg, P and Shore, N D and Demirhan, E and Modelska, K and Phung, D and Krivoshik, A and Sternberg, C N        | PROSPER: a phase 3, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (M0 CRPC)                                                                                                                                 | Journal of clinical oncology              | 2018 | 36      | 6      |           | Tipo de publicación equivocada |
| Hussain, M and Fizazi, K and Saad, F and Rathenborg, P and Shore, N D and Demirhan, E and Modelska, K and Phung, D and Krivoshik, A and Sternberg, C N        | PROSPER: a phase 3, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) in men with nonmetastatic castration-resistant prostate cancer (M0 CRPC)                                                                                                                                 | Journal of clinical oncology              | 2018 | 36      | 6      |           | Tipo de publicación equivocada |
| Gurney, H and Hussain, M and Fizazi, K and Saad, F and Rathenborg, P and Shore, N D and Demirhan, E and Modelska, K and Phung, D and Krivoshik, A and al., et | Prosper: a phase 3, randomised, double-blind, placebo-controlled study of enzalutamide in menwith non-metastatic castration-resistant prostate cancer (NMCRPC)                                                                                                                                               | Asia-Pacific journal of clinical oncology | 2018 | 14      |        | 34-35     | Tipo de publicación equivocada |

## Anexo H. Evaluación de la calidad (riesgo de sesgos)

**Tabla H-1. Riesgo de sesgos de los ECA incluidos en la pregunta 1.**

| Estudio     | Autor/año   | Outcome      | Weight | D1 | D2 | D3 | D4 | D5 | Overall |   |
|-------------|-------------|--------------|--------|----|----|----|----|----|---------|---|
| EORTC 22863 | Bolla 2010  | OS, MFS, PFS | 1      | !  | +  | +  | +  | +  | +       | + |
| ASD         | Sargos 2020 | AS           | 1      | +  | +  | +  | +  | +  | +       | + |

 Low risk  
 Some concerns  
 High risk

D1 Randomisation process  
 D2 Deviations from the intended interventions  
 D3 Missing outcome data  
 D4 Measurement of the outcome  
 D5 Selection of the reported result

**Tabla H-2. Riesgo de sesgos de los ECA incluidos en la pregunta 2.**

| Estudio | Autor/año    | Outcome               | Weight | D1 | D2 | D3 | D4 | D5 | Overall |   |
|---------|--------------|-----------------------|--------|----|----|----|----|----|---------|---|
| PROSPER | Hussain 2018 | OS, MFS, PFS PSA, SAG | 1      | +  | +  | +  | +  | +  | +       | + |
| SPARTAN | Smith 2018   | OS, MFS, PFS PSA, SAG | 1      | +  | +  | +  | +  | +  | +       | + |
| ARAMIS  | Fizazi 2019  | OS, MFS, PFS PSA, SAG | 1      | +  | +  | +  | +  | +  | +       | + |
| STRIVE  | Penson 2016  | PFS PSA               | 1      | +  | +  | +  | +  | +  | +       | + |

 Low risk  
 Some concerns  
 High risk

D1 Randomisation process  
 D2 Deviations from the intended interventions  
 D3 Missing outcome data  
 D4 Measurement of the outcome  
 D5 Selection of the reported result

**Tabla H-3. Riesgo de sesgos de los ECA incluidos en la pregunta 3.**

| Estudio                   | Autor / año          | Outcome          | Weight | D1 | D2 | D3 | D4 | D5 | Overall |   |
|---------------------------|----------------------|------------------|--------|----|----|----|----|----|---------|---|
| Casodex Combination Study | Schellhammer P 1995  | OS, TTF, PFS, EA | 1      | +  | +  | !  | +  | +  | !       | + |
| Casodex Combination Study | Schellhammer P 1996  | OS, TTP, PFS     | 1      | +  | +  | !  | +  | !  | !       | ! |
| KYUCOG-1401               | Yokomizo A 2024      | OS, PFS, EA      | 1      | +  | !  | +  | +  | !  | !       | ! |
| Intergroup 0036           | Crawford ED 1989     | OS, PFS, EA      | 1      | +  | !  | +  | +  | +  | +       | + |
| Casodex Combination Study | Schellhammer PF 1997 | OS, TTP, PFS, EA | 1      | +  | +  | !  | +  | !  | !       | ! |
| CASODEX factorial         | Sarosdy MF 1998      | OS, PFS, EA      | 1      | +  | !  | +  | +  | !  | !       | ! |
| JAMA Oncol Trial          | Vaishampayan U 2021  | OS, TTP, PFS, EA | 1      | +  | +  | !  | !  | +  | !       | ! |
| ARCHES                    | Armstrong AJ 2019    | OS, PFS, EA      | 1      | +  | +  | !  | +  | +  | +       | + |
| ENZAMET                   | Davis ID 2019        | OS, PFS, EA      | 1      | +  | +  | +  | !  | +  | +       | + |
| LATITUDE                  | Fizazi K 2017        | OS, PFS, EA      | 1      | +  | +  | !  | +  | +  | +       | + |
| PEACE-1                   | Fizazi K 2022        | OS, PFS, EA      | 1      | +  | !  | +  | !  | +  | !       | ! |
| TITAN                     | Chi KN 2019          | OS, PFS, EA      | 1      | +  | +  | +  | +  | !  | +       | + |
| STAMPEDE - Arm G          | James ND 2017        | OS, PFS, EA      | 1      | +  | +  | !  | !  | +  | !       | ! |

 Low risk  
 Some concerns  
 High risk

D1 Randomisation process  
 D2 Deviations from the intended interventions  
 D3 Missing outcome data  
 D4 Measurement of the outcome  
 D5 Selection of the reported result

**Tabla H-4. Riesgo de sesgos de los ECA incluidos en la pregunta 4.**

| Estudio  | Autor / año      | Weight | D1 | D2 | D3 | D4 | D5 | Overall |   |
|----------|------------------|--------|----|----|----|----|----|---------|---|
| ALSYMPCA | Parker 2013      | 1      | +  | !  | +  | +  | +  | !       | + |
| VISION   | Sartor 2021      | 1      | +  | +  | +  | +  | +  | +       | + |
| PROfound | Bono 2020        | 1      | +  | !  | +  | +  | +  | !       | ! |
| ABIDO    | Cilment 2022     | 1      | +  | !  | +  | +  | +  | !       | ! |
| CARD     | De Wit 2019      | 1      | +  | !  | +  | +  | !  | !       | ! |
| PRESIDE  | Merseburger 2022 | 1      | +  | +  | +  | +  | +  | +       | + |

 Low risk  
 Some concerns  
 High risk

D1 Randomisation process  
 D2 Deviations from the intended interventions  
 D3 Missing outcome data  
 D4 Measurement of the outcome  
 D5 Selection of the reported result

**Tabla H-5. Valoración de riesgo de sesgo RSL con herramienta ROBIS**

| N. | Título                                                                                                                                                                                                                               | Autor y año       | Dominio 1 | Dominio 2 | Dominio 3 | Dominio 4 | General |   |
|----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-----------|-----------|-----------|-----------|---------|---|
| 1  | Androgen deprivation therapy use and duration with definitive radiotherapy for localised prostate cancer: an individual patient data meta-analysis                                                                                   | Kishan, 2022      | ●         | ●         | ●         | ●         | ●       | a |
| 2  | Health-related quality of life outcomes in randomized controlled trials in metastatic hormone-sensitive prostate cancer: a systematic review                                                                                         | Osanto, 2024      | ●         | ●         | ●         | ●         | ●       | b |
| 3  | Toxicities of radioligand and radioisotope therapy in prostate cancer: a systematic review and meta análisis                                                                                                                         | Ventura, 2025     | ●         | ●         | ●         | ●         | ●       | c |
| 4  | Comparative efficacy of Olaparib in combination with or without novel antiandrogens for treating metastatic castration-resistant prostate cancer                                                                                     | Chen, 2023        | ●         | ●         | ●         | ●         | ●       | d |
| 5  | The Efficacyof Cabazitaxel in Treating Prostate Cancer: A Systematic Review and Meta-Analysis                                                                                                                                        | Hashim, 2024      | ●         | ●         | ●         | ●         | ●       | e |
| 6  | A Meta-Analysis of Randomized Clinical Trials Assessing the Efficacy of PARP Inhibitors in Metastatic Castration-Resistant Prostate Cancer                                                                                           | Alameddine, 2023  | ●         | ●         | ●         | ●         | ●       | f |
| 7  | Safety profile of darolutamide versus placebo: a systematic review and meta-analysis                                                                                                                                                 | Turco, 2024       | ●         | ●         | ●         | ●         | ●       | g |
| 8  | Cabazitaxel versus abiraterone or enzalutamide for metastatic castration-resistant prostate cancer following docetaxel failure: a systematic review and meta-analysis                                                                | Da Silva, 2025    | ●         | ●         | ●         | ●         | ●       | h |
| 9  | Evaluation of the Efficacy of PARP Inhibitors in Metastatic Castration-Resistant Prostate Cancer: A Systematic Review and Meta-Analysis                                                                                              | Wu 2021           | ●         | ●         | ●         | ●         | ●       | i |
| 10 | Overall Survival and Safety of Men with Metastatic Hormone-Sensitive Prostate Cancer Treated with Combination Therapy of Novel Androgen Receptor Antagonists and Androgen-Deprivation Therapy: A Systematic Review and Meta-Analysis | Wu 2022           | ●         | ●         | ●         | ●         | ●       | j |
| 11 | Central Nervous System Toxicity in Prostate Cancer Patients Treated with Androgen Receptor Signaling Inhibitors: A Systematic Review, Meta-analysis, and Network Meta-analysis                                                       | Matsukawa, 2025-2 | ●         | ●         | ●         | ●         | ●       | k |
| 12 | Health-related quality of life in patients with metastatic hormone-sensitive prostate cancer treated with androgen receptor signaling inhibitors: the role of combination treatment therapy                                          | Afferi, 2024      | ●         | ●         | ●         | ●         | ●       | l |
| 13 | Efficacy and safety of PARP inhibitors in prostate cancer: An umbrellareview of systematic reviews and meta-analyse                                                                                                                  | Tzang 2025        | ●         | ●         | ●         | ●         | ●       | m |
| 14 | Androgen deprivation therapy use and duration with definitive radiotherapy for localised prostate cancer: an individual patient data meta-analysis                                                                                   | Kishan, 2022      | ●         | ●         | ●         | ●         | ●       | n |
| 15 | Health-related quality of life outcomes in randomized controlled trials in metastatic hormone-sensitive prostate cancer: a systematic review                                                                                         | Osanto, 2024      | ●         | ●         | ●         | ●         | ●       | o |
| 16 | Toxicities of radioligand and radioisotope therapy in prostate cancer: a systematic review and meta análisis                                                                                                                         | Ventura, 2025     | ●         | ●         | ●         | ●         | ●       | p |
| 17 | Comparative efficacy of Olaparib in combination with or without novel antiandrogens for treating metastatic castration-resistantprostate cancer                                                                                      | Chen, 2023        | ●         | ●         | ●         | ●         | ●       | q |
| 18 | The Efficacyof Cabazitaxel in Treating Prostate Cancer: A Systematic Review and Meta-Analysis                                                                                                                                        | Hashim, 2024      | ●         | ●         | ●         | ●         | ●       | r |
| 19 | A Meta-Analysis of Randomized Clinical Trials Assessing the Efficacy of PARP Inhibitors in Metastatic Castration-Resistant Prostate Cancer                                                                                           | Alameddine, 2023  | ●         | ●         | ●         | ●         | ●       | s |
| 20 | Safety profile of darolutamide versus placebo: a systematic review and meta-analysis                                                                                                                                                 | Turco, 2024       | ●         | ●         | ●         | ●         | ●       | t |

| N. | Título                                                                                                                                                                                                                            | Autor y año            | Dominio 1 | Dominio 2 | Dominio 3 | Dominio 4 | General |    |
|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------|-----------|-----------|-----------|---------|----|
| 21 | Cabazitaxel versus abiraterone or enzalutamide for metastatic castration-resistant prostate cancer following docetaxel failure: a systematic review and meta-analysis                                                             | Da Silva, 2025         | ●         | ●         | ●         | ●         | ●       | u  |
| 22 | A meta-analysis on overall survival and safety outcomes in patients with nonmetastatic castration-resistant prostate cancer treated with novel hormonal agents                                                                    | Rizzo et al, (2021)    | ●         | ●         | ●         | ●         | ●       | v  |
| 23 | A Systematic Review and MetaAnalysis of Randomized Controlled Trials With Novel Hormonal Therapies for Non-Metastatic Castration-Resistant Prostate Cancer: An Update From Mature Overall Survival Data                           | Maggi et al, (2021)    | ●         | ●         | ●         | ●         | ●       | w  |
| 24 | A systematic review and meta-analysis on non-metastatic castration-resistant prostate cancer: The radiation oncologist's perspective                                                                                              | Ingrosso et al, (2022) | ●         | ●         | ●         | ●         | ●       | x  |
| 25 | Enzalutamide vs Abiraterone in Castration Resistant Prostate Cancer: Indirect Comparison of Treatments                                                                                                                            | Poveda et al, (2019)   | ●         | ●         | ●         | ●         | ●       | y  |
| 26 | Incidence and Risk of Thromboembolic and Cardiovascular Adverse Events with PARP Inhibitor Treatment in Patients with mCRPC: A Systematic Review and Safety Meta-analysis                                                         | Maiorano et al, (2025) | ●         | ●         | ●         | ●         | ●       | z  |
| 27 | First-line systemic therapy for metastatic castration-sensitive prostate cancer: An updated systematic review with novel findings                                                                                                 | Ferro et al, (2021)    | ●         | ●         | ●         | ●         | ●       | aa |
| 28 | Evaluation of maintenance of the common androgen deprivation therapy with the new antiandrogen therapy in patients with castration-resistant prostate cancer: a systematic review                                                 | Salgado 2022           | ●         | ●         | ●         | ●         | ●       |    |
| 29 | Comparison of Systemic Treatments for Metastatic Castration-Sensitive Prostate Cancer A Systematic Review and Network Meta-analysis                                                                                               | Wang 2021              | ●         | ●         | ●         | ●         | ●       |    |
| 30 | Meta-analysis to evaluate the comparative effectiveness of enzalutamide and abiraterone acetate for first-line treatment of metastatic castration-resistant prostate cancer in realworld settings                                 | Aprikian, 2025         | ●         | ●         | ●         | ●         | ●       |    |
| 31 | A Meta-Analysis and Meta-Regression of the Efficacy, Toxicity, and Quality of Life Outcomes Following Prostate-Specific Membrane Antigen Radioligand Therapy Utilising Lutetium-177 and Actinium225 in Metastatic Prostate Cancer | Dai 2024               | ●         | ●         | ●         | ●         | ●       |    |
| 32 | Comparative therapeutic efficacy and safety of first-line and second-line therapies for metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis                                            | Jiang 2025             | ●         | ●         | ●         | ●         | ●       |    |
| 33 | Comparative effectiveness of first-line systemic treatments for metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis                                                                    | Ai 2024                | ●         | ●         | ●         | ●         | ●       |    |
| 34 | Comparison of Systemic Treatments for Metastatic Castration-Resistant Prostate Cancer After Docetaxel Failure: A Systematic Review and Network Meta-analysis                                                                      | Chen 2021              | ●         | ●         | ●         | ●         | ●       |    |
| 35 | Evaluating first-line therapeutic strategies for metastatic castration-resistant prostate cancer: a comprehensive network meta-analysis and systematic review                                                                     | Zhang 2024             | ●         | ●         | ●         | ●         | ●       |    |
| 36 | Second-line treatment options in metastatic castration-resistant prostate cancer after progression on first-line androgen-receptor targeting therapies: A systematic review and Bayesian network analysis                         | Xiong 2024             | ●         | ●         | ●         | ●         | ●       |    |
| 37 | Comparative Efficacy of Combined Radiotherapy, Systemic Therapy, and Androgen Deprivation Therapy for Metastatic Hormone-Sensitive Prostate Cancer: A Network Meta-Analysis and Systematic Review                                 | Wang 2020              | ●         | ●         | ●         | ●         | ●       |    |
| 38 | The efficacy and safety of PARP inhibitors in mCRPC with HRR mutation in second-line treatment: a systematic review and bayesian network meta-analysis                                                                            | Zhu 2024               | ●         | ●         | ●         | ●         | ●       |    |
| 39 | PARP Inhibitors in Metastatic Prostate Cancer: A Comprehensive Systematic Review and Meta-analysis of Existing Evidence                                                                                                           | Ditunno 2024           | ●         | ●         | ●         | ●         | ●       |    |
| 40 | Optimal treatment sequencing of abiraterone acetate plus prednisone and enzalutamide in patients with castration-resistant metastatic prostate cancer: A systematic review and meta-analysis                                      | Casinello 2021         | ●         | ●         | ●         | ●         | ●       |    |

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| <p>a. Aunque se trata de un metaanálisis de datos individuales de ensayos clínicos aleatorizados multicéntricos, lo que constituye una fortaleza metodológica, se identificaron limitaciones importantes en varios aspectos clave: los criterios de elegibilidad incluyeron restricciones (idioma, exclusión de estudios de un solo centro o con TPA indefinida) que reducen la exhaustividad de la evidencia; la estrategia de búsqueda no fue completamente transparente ni exhaustiva, lo que aumenta el riesgo de sesgo de publicación; la evaluación del riesgo de sesgo de los estudios primarios no se realizó con una herramienta estandarizada ni se reportó de forma clara el número de revisores involucrados; y en la síntesis e interpretación de resultados no se integró el riesgo de sesgo de los estudios, ni se discutieron de forma suficiente las limitaciones metodológicas identificadas.</p> <p>b. La revisión siguió un protocolo registrado en PROSPERO, utilizó una búsqueda estructurada en múltiples bases de datos, aplicó procesos en duplicado y evaluó el riesgo de sesgo con la herramienta RoB 2, sin embargo, se identifican limitaciones metodológicas como la restricción por idioma (solo inglés) y por fecha (desde 2015) pueden haber reducido la exhaustividad de la evidencia. La gran heterogeneidad entre los estudios en los instrumentos de HRQoL, tiempos de evaluación y formas de reporte impidió realizar un metaanálisis, limitando la robustez de la síntesis.</p> |                                                                                                                                                                                                                                        |                        |           |           |           |           |         |    |

- c. Si bien la revisión siguió PRISMA, aplicó criterios de inclusión claros, usó procedimientos de extracción de datos en consenso y realizó una síntesis estadística con métodos apropiados (modelos de efectos aleatorios, GLMM,  $I^2$ , funnel plots), se identificaron limitaciones metodológicas importantes. Entre ellas destacan la búsqueda restringida a solo dos bases de datos y a estudios en inglés, la ausencia de un protocolo registrado, y la inclusión mayoritaria de estudios retrospectivos, lo que reduce la solidez y generalización de los resultados. Además, aunque se evaluó la calidad de los estudios con la escala NOS, esta no se integró de manera sistemática en la interpretación de la evidencia, y persiste el riesgo de sesgo de publicación.
- d. La revisión presenta varias fortalezas: criterios de elegibilidad claros, protocolo registrado en INPLASY, búsqueda en bases de datos principales, inclusión de ensayos clínicos aleatorizados de alta calidad y uso de la herramienta Cochrane para evaluar riesgo de sesgo. Sin embargo, persisten limitaciones relevantes: la restricción a estudios en inglés, la ausencia de búsqueda en literatura gris, y la dependencia de pocos ensayos con comparaciones indirectas y desenlaces aún inmaduros, lo que reduce la solidez de las conclusiones.
- e. La revisión tiene varias fortalezas: protocolo registrado en PROSPERO, búsqueda en múltiples bases de datos relevantes, criterios de elegibilidad claros, inclusión de desenlaces clínicamente pertinentes y aplicación de métodos estadísticos robustos (modelos de efectos aleatorios, análisis de subgrupos y sensibilidad). Además, se utilizó la herramienta RoB 2.0 para evaluar el riesgo de sesgo de los estudios primarios. Sin embargo, persisten limitaciones importantes: la restricción a estudios en inglés y de texto completo, la no inclusión de literatura gris, la falta de claridad sobre si la selección y evaluación se realizaron en duplicado y la alta heterogeneidad en algunos resultados (p. ej., eventos adversos). Estas debilidades reducen la confianza en la exhaustividad y en la solidez de las conclusiones.
- f. La combinación de limitaciones metodológicas en la definición de criterios, identificación de estudios y síntesis de resultados indica que la confianza en los hallazgos es reducida, por lo que la revisión presenta un alto riesgo de sesgo.
- g. No se registró un protocolo, la búsqueda fue limitada y sin literatura gris, los desenlaces analizados se restringieron a ciertos eventos adversos y no se realizaron análisis de sensibilidad ni evaluación formal del sesgo de publicación.
- h. Debido a la heterogeneidad en la calidad de los estudios incluidos y a posibles sesgos de publicación que podrían influir en la robustez de las conclusiones.
- i. El riesgo de sesgo de selección se calificó como moderado, porque seis de los nueve ensayos clínicos incluidos eran estudios de un solo brazo.
- j. El riesgo de sesgo se justifica principalmente por las limitaciones de la calidad metodológica de los estudios primarios que se incluyeron en la revisión.
- k. La fase 2 identificó preocupaciones en cuanto a la restricción por idioma y a la falta de especificación en cómo se realizó la selección por texto completo, sin embargo, se considera que la búsqueda en idioma inglés permite recuperar evidencia relevante para responder la pregunta de investigación y que, teniendo en cuenta que la tamización por título y resumen, la extracción de datos y la evaluación del riesgo de sesgo de hizo de forma independiente y pareada, la selección por texto completo también.
- l. La metodología para realizar la RSL no se describe de forma detallada, se aplicaron restricciones que no fueron justificadas; el proceso de selección, recolección de datos y evaluación del riesgo de sesgos no es claro. Los resultados de la RSL no abordan los resultados obtenidos al realizar la evaluación del riesgo de sesgo.
- m. Los criterios de elegibilidad se mencionan de forma detallada, la metodología para la búsqueda y selección de estudios y extracción de datos también se describe de forma detallada. De igual forma se menciona como se propuso realizar la síntesis de evidencia. Se realizó la evaluación de la calidad de la evidencia, con variabilidad en las calificaciones.
- n. Aunque se trata de un metaanálisis de datos individuales de ensayos clínicos aleatorizados multicéntricos, lo que constituye una fortaleza metodológica, se identificaron limitaciones importantes en varios aspectos clave: los criterios de elegibilidad incluyeron restricciones (idioma, exclusión de estudios de un solo centro o con TPA indefinida) que reducen la exhaustividad de la evidencia; la estrategia de búsqueda no fue completamente transparente ni exhaustiva, lo que aumenta el riesgo de sesgo de publicación; la evaluación del riesgo de sesgo de los estudios primarios no se realizó con una herramienta estandarizada ni se reportó de forma clara el número de revisores involucrados; y en la síntesis e interpretación de resultados no se integró el riesgo de sesgo de los estudios, ni se discutieron de forma suficiente las limitaciones metodológicas identificadas.
- o. La revisión siguió un protocolo registrado en PROSPERO, utilizó una búsqueda estructurada en múltiples bases de datos, aplicó procesos en duplicado y evaluó el riesgo de sesgo con la herramienta RoB 2, sin embargo, se identifican limitaciones metodológicas como la restricción por idioma (solo inglés) y por fecha (desde 2015) pueden haber reducido la exhaustividad de la evidencia. La gran heterogeneidad entre los estudios en los instrumentos de HRQoL, tiempos de evaluación y formas de reporte impidió realizar un metaanálisis, limitando la robustez de la síntesis.
- p. Si bien la revisión siguió PRISMA, aplicó criterios de inclusión claros, usó procedimientos de extracción de datos en consenso y realizó una síntesis estadística con métodos apropiados (modelos de efectos aleatorios, GLMM,  $I^2$ , funnel plots), se identificaron limitaciones metodológicas importantes. Entre ellas destacan la búsqueda restringida a solo dos bases de datos y a estudios en inglés, la ausencia de un protocolo registrado, y la inclusión mayoritaria de estudios retrospectivos, lo que reduce la solidez y generalización de los resultados. Además, aunque se evaluó la calidad de los estudios con la escala NOS, esta no se integró de manera sistemática en la interpretación de la evidencia, y persiste el riesgo de sesgo de publicación.
- q. La revisión presenta varias fortalezas: criterios de elegibilidad claros, protocolo registrado en INPLASY, búsqueda en bases de datos principales, inclusión de ensayos clínicos aleatorizados de alta calidad y uso de la herramienta Cochrane para evaluar riesgo de sesgo. Sin embargo, persisten limitaciones relevantes: la restricción a estudios en inglés, la ausencia de búsqueda en literatura gris, y la dependencia de pocos ensayos con comparaciones indirectas y desenlaces aún inmaduros, lo que reduce la solidez de las conclusiones.



- r. La revisión tiene varias fortalezas: protocolo registrado en PROSPERO, búsqueda en múltiples bases de datos relevantes, criterios de elegibilidad claros, inclusión de desenlaces clínicamente pertinentes y aplicación de métodos estadísticos robustos (modelos de efectos aleatorios, análisis de subgrupos y sensibilidad). Además, se utilizó la herramienta RoB 2.0 para evaluar el riesgo de sesgo de los estudios primarios. Sin embargo, persisten limitaciones importantes: la restricción a estudios en inglés y de texto completo, la no inclusión de literatura gris, la falta de claridad sobre si la selección y evaluación se realizaron en duplicado y la alta heterogeneidad en algunos resultados (p. ej., eventos adversos). Estas debilidades reducen la confianza en la exhaustividad y en la solidez de las conclusiones.
- s. La combinación de limitaciones metodológicas en la definición de criterios, identificación de estudios y síntesis de resultados indica que la confianza en los hallazgos es reducida, por lo que la revisión presenta un alto riesgo de sesgo.
- t. No se registró un protocolo, la búsqueda fue limitada y sin literatura gris, los desenlaces analizados se restringieron a ciertos eventos adversos y no se realizaron análisis de sensibilidad ni evaluación formal del sesgo de publicación.
- u. Debido a la heterogeneidad en la calidad de los estudios incluidos y a posibles sesgos de publicación que podrían influir en la robustez de las conclusiones.
- v. Metodológicamente, es sólido, con los tres ECA s (SPARTAN, PROSPER, ARAMIS) evaluados como de bajo riesgo de sesgo mediante la herramienta Cochrane, y la síntesis usando modelos fijos/aleatorios ( $I^2=0\%$  para OS,  $I^2=89\%$  para ADEs) respaldada por gráficos de funnel simétricos. Sin embargo, los riesgos clave incluyen: la ausencia de análisis de sensibilidad, que debilita la robustez ante la alta heterogeneidad en ADEs.
- w. Se empleó una metodología rigurosa: recolección multipaso con criterios PICO, aunque sin resolución explícita de discrepancias; selección de tres ECA (2009-2020) vía Medline/Cochrane/ASCO, relevante para M0 CRPC; características suficientes (diseño fase III, OS, AEs), con datos secundarios ausentes; y síntesis pooled (HR, ERs) con random effects para  $I^2>50\%$ , con bajo RoB por Cochrane, pero sin sensibilidad, donde no abordan todas limitaciones, sugiriendo riesgo moderado mitigado por calidad inicial.
- x. El estudio presenta una metodología sólida y acorde con los estándares internacionales para revisiones sistemáticas y metaanálisis, apoyando la validez, reproducibilidad y aplicabilidad clínica de sus resultados y conclusiones, si bien podría mejorar en la transparencia del registro de protocolo y reporte de análisis predefinidos.
- y. El estudio realizó una revisión sistemática con búsqueda en PubMed, EMBASE y Cochrane, incluyendo ensayos fase III y evaluando riesgo de sesgo con criterios Cochrane. Aplicó el modelo estadístico de Bucher para comparaciones indirectas entre enzalutamida y abiraterona, usando software especializado. Su fortaleza radica en la solidez metodológica y la pertinencia clínica del análisis; sin embargo, la ausencia de comparaciones directas y la heterogeneidad entre poblaciones limitan la validez externa de los resultados.
- z. Revisión sistemática y metaanálisis sobre inhibidores de PARP en cáncer de próstata resistente a la castración. Incluyó estudios relevantes con modelos de efectos aleatorios para estimar riesgos agrupados. Aporta evidencia robusta, pero la heterogeneidad de poblaciones y la falta de análisis profundo de sesgo de publicación reducen la certeza de los resultados.
- aa. Revisión sistemática y metaanálisis en red bajo PRISMA, con ensayos clínicos fase III que compararon ARAT y docetaxel en combinación con ADT. Se evaluó calidad con escala Jadad y riesgo de sesgo con herramienta Cochrane, usando modelos de efectos aleatorios. La metodología es rigurosa, aunque la inclusión de ensayos abiertos y la heterogeneidad clínica limitan la solidez de las conclusiones.
- ab. RSL con búsqueda tricompartida, doble revisión, uso formal de Cochrane RoB y NMA bayesiana; sin registro PROSPERO ni evaluación de sesgo de publicación.
- ac. RSL con búsqueda tricompartida, doble revisión y uso formal de Cochrane RoB; modelo bayesiano robusto, sin evaluación de sesgo de publicación ni registro PROSPERO.
- ad. Actualización de NMA previa; criterios y búsqueda adecuados, pero sin detalle de doble extracción ni evaluación formal de sesgo; síntesis adecuada aunque limitada en transparencia.
- ae. Actualización que integra ARANOTE; criterios claros, pero sin nuevo protocolo ni registro PROSPERO; extracción no doble y sin reporte de sesgo; análisis frecuentista coherente con publicaciones previas.
- af. RSL con NMA bayesiana; criterios y extracción doble adecuados; sin registro PROSPERO ni sesgo de publicación evaluado, aunque análisis de consistencia y sensibilidad apropiados.
- ag. RSL y NMA con registro PRISMA, doble revisión, RoB2 por dominio y análisis de heterogeneidad; riesgo de sesgo bajo en todos los dominios.
- ah. NMA con protocolo PRISMA, doble revisión, RoB2, heterogeneidad y SUCRA; riesgo bajo en todos los dominios.
- ai. RSL y NMA bayesiana con búsqueda amplia, doble revisión y RoB2; análisis de consistencia y heterogeneidad completos; riesgo bajo en todos los dominios.
- aj. RSL y NMA bayesiana con doble revisión, RoB2 y PRISMA; sin evaluación formal de sesgo de publicación, aunque consistencia y sensibilidad adecuadas.
- ak. SR viva + NMA; búsqueda desde inicio y auto-updates; doble extracción y RoB2; NMA fija por red abierta; subgrupos por volumen y sincronía; sin pruebas formales de inconsistencia/sesgo de publicación en la NMA.
- al. Revisión sistemática y NMA bayesiana registrada en PROSPERO; búsqueda hasta 2024 con inclusión de conferencias; doble extracción y RoB2, riesgo de sesgo bajo en todos los dominios.
- am. Revisión PRISMA con búsqueda exhaustiva; extracción y RoB2 duplicados; NMA frecuentista en R; sin evaluación formal de inconsistencia ni sesgo de publicación; resultados consistentes en OS y PFS.
- an. Meta-análisis PRISMA sobre grupos control de ECA en mHSPC; búsqueda exhaustiva; análisis de supervivencia con modelo no paramétrico; alta heterogeneidad; sin RoB formal ni metarregresión multivariada; riesgo global moderado.



ao. Revisión PRISMA de 8 ECA fase III en mHSPC ( n = 9987 ); evalúa OS, rPFS, bPFS y AEs  $\geq$  G3; emplea RoB Cochrane; alta heterogeneidad en subgrupos; riesgo global moderado

Fuente: elaboración propia

**Tabla H-6. Valoración de riesgo de sesgo RSL con MAR con herramienta IQWiG**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                                                                                                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| Estudio: Mutlu 2021 — <i>The optimal upfront therapy in metastatic hormone-sensitive prostate cancer: A network meta-analysis</i> (2)                                                        |           |                                                                                                                                                   |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                                                                                                   |
|                                                                                                                                                                                              | Juicio    | Justificación                                                                                                                                     |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Objetivo explícito de identificar la terapia óptima en mHSPC mediante NMA. Se declara como meta del estudio.                                      |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Parcial   | Se infiere por múltiples opciones sin comparaciones directas completas; la justificación explícita es breve.                                      |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Parcial   | La red pivota en ADT como nodo, pero la razón de preferir red sobre comparaciones directas no se discute en detalle.                              |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | Bases (PubMed, Web of Science), ClinicalTrials.gov, congresos ASCO/ESMO, Google; periodo y criterios descritos.                                   |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | Ensayos fase III de primera línea mHSPC con OS; resolución de discrepancias entre revisores.                                                      |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Tabla de características/HR por estudio, grafo de red y resultados por desenlace; se muestran HRs comparativos.                                   |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Parcial   | Se usó modelo de consistencia y se evaluó heterogeneidad (funnel/ajuste), pero sin pruebas detalladas de inconsistencia (p. ej., node-splitting). |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | NMA bayesiana con GeMTC, especificación (Poisson/log), burn-in/iteraciones, manejo de SE/HR; referencias metodológicas.                           |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Parcial   | Se comentan alcances y comparabilidad; la discusión de transitividad/consistencia es limitada en el texto disponible.                             |

**Valoración global: Buena** fortalezas en búsqueda y método; justificar mejor supuestos de transitividad/consistencia

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |              |                                                                                                                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|-------------------------------------------------------------------------------------------------------------------|
| Mori 2020 — Apalutamide, enzalutamide, and darolutamide for non-metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis (3)                           |              |                                                                                                                   |
| Criterio                                                                                                                                                                                     | KC<br>Juicio | Justificación                                                                                                     |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí           | Objetivo/alcance definidos (nmCRPC; MFS/OS) y estructura de protocolo metodológico en secciones de métodos.       |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí           | Justifica NMA por ausencia de comparaciones directas entre ARPIs en nmCRPC. (Implícito en red multi-tratamiento). |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Parcial      | El comparador común (placebo/ADT estándar) se asume; la preferencia por red vs directa no se discute ampliamente. |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí           | Estrategia de búsqueda y flujo PRISMA-NMA referenciados.                                                          |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí           | Inclusión: ECA nmCRPC; extracción y evaluación de sesgo definidas (Cochrane RoB).                                 |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí           | Presenta estudios, red y resultados por desenlace                                                                 |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí           | Marco de NMA (consistencia, homogeneidad)                                                                         |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí           | Herramientas y referencias técnicas claramente citadas.                                                           |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí           | Limitaciones metodológicas y clínicas discutidas en discusión                                                     |

**Valoración global: Alta** (muy sólido en método y reporte PRISMA-NMA)

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |        |                                                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|----------------------------------------------------------------------------------------------------|
| Mori 2022 — Systemic therapies for metastatic hormone-sensitive prostate cancer: network meta-analysis (4)                                                                                   |        |                                                                                                    |
| Criterio                                                                                                                                                                                     | KC     |                                                                                                    |
|                                                                                                                                                                                              | Juicio | Justificación                                                                                      |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí     | Pregunta/alcance establecidos                                                                      |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí     | Justificación de NMA explícita en contexto de ausencia de comparaciones directas completas.        |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí     | Comparador común (ADT/placebo) en red justificado por marco frequentista.                          |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí     | Sigue PRISMA-NMA; búsqueda y selección descritas.                                                  |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí     | Criterios predefinidos; evalúa riesgo de sesgo (Cochrane).                                         |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí     | Reporte de características, red y estimaciones (con IC) y metaanálisis en parejas cuando aplica.   |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí     | Investiga homogeneidad/consistencia y discute supuestos; ranking frequentista (p-scores).          |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí     | Herramientas adecuadas (frequentista), detalles técnicos y referencias (Rücker/Schwarzer; log-HR). |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí     | Limitaciones (datos agregados, indirectitud, etc.) discutidas.                                     |

**Valoración global: Alta**, justifica muy bien todos los aspectos metodológicos.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |         |                                                                                                  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|--------------------------------------------------------------------------------------------------|
| Wang 2021 – Comparison of Systemic Treatments for Metastatic Castration-Sensitive Prostate Cancer A Systematic Review and Network Meta-analysis (5)                                          |         |                                                                                                  |
| Criterio                                                                                                                                                                                     | KC      | Justificación                                                                                    |
|                                                                                                                                                                                              | Juicio  |                                                                                                  |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí      | Pregunta definida (comparar tratamientos sistémicos mCSPC).                                      |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí      | NMA justificada por múltiples opciones y escasez de comparaciones directas completas.            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Parcial | Comparador común (SOC/ADT) implícito; poca discusión comparador-común vs comparaciones directas. |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí      | Enfoque PRISMA reportado/citado; revisión sistemática previa al NMA.                             |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí      | Criterios preespecificados (ECA mCSPC; desenlaces); proceso de selección descrito.               |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí      | Reporte de características, red y estimaciones por tratamiento/desenlace.                        |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí      | Supuestos y evaluaciones metodológicas (consistencia/homogeneidad) citando guías PRISMA-NMA/ROB. |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí      | Herramientas y técnicas apropiadas (log-HR, manejo de ensayos multi-brazo).                      |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí      | Limitaciones discutidas (p.ej., datos agregados; heterogeneidad clínica).                        |

**Valoración global: Alta**, aspectos metodológicos robustos.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)            |        |                                                                                                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|---------------------------------------------------------------------------------------------------|
| Jiang 2025 — Comparative therapeutic efficacy and safety of first-line and second-line therapies for metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis (6) |        |                                                                                                   |
| Criterio                                                                                                                                                                                                | KC     |                                                                                                   |
|                                                                                                                                                                                                         | Juicio | Justificación                                                                                     |
| 1. ¿Pregunta a priori?                                                                                                                                                                                  | Sí     | Pregunta y alcances definidos (tratamientos en mCRPC).                                            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                               | Sí     | Justifica NMA por múltiples intervenciones y falta de comparaciones directas completas.           |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                              | Sí     | Comparador común explicado por estructura de red; coherencia con guías.                           |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                        | Sí     | PRISMA-NMA citado; flujo y materiales suplementarios.                                             |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                          | Sí     | Criterios predefinidos y selección reproducible.                                                  |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                               | Sí     | Red, geometría y resultados por comparaciones; materiales suplementarios.                         |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                            | Sí     | Evalúa consistencia (herramientas gráficas de inconsistencia) y suposiciones; lo declara en refs. |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                               | Sí     | Código de programación disponible (GitHub), detalles técnicos transparentes.                      |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                | Sí     | Limitaciones metodológicas y de base de datos discutidas.                                         |

**Valoración global: Alta**, muy transparente; códigos publicados.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |         |                                                                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|--------------------------------------------------------------------------------------------------------------------|
| Matsukawa 2025 — Cardiovascular events among men with prostate cancer treated with androgen receptor signaling inhibitors: a systematic review, meta-analysis, and network meta-analysis (7) |         |                                                                                                                    |
| Criterio                                                                                                                                                                                     | KC      |                                                                                                                    |
|                                                                                                                                                                                              | Juicio  | Justificación                                                                                                      |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí      | Pregunta definida (AEs CV con ARPIs; NMA).                                                                         |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí      | NMA justificada para comparar seguridad entre múltiples ARPIs.                                                     |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Parcial | Comparador común implícito; la elección frente a comparaciones directas se discute poco en el extracto disponible. |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí      | PRISMA indicado; revisión sistemática previa.                                                                      |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí      | Criterios de inclusión/exclusión establecidos para ECA de ARPIs.                                                   |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí      | Características de estudios y estimaciones presentadas; geometría de la red descrita.                              |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Parcial | Evaluación de heterogeneidad/consistencia probable; detalle limitado.                                              |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí      | Técnicas NMA adecuadas para seguridad; referencias metodológicas estándar.                                         |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí      | Limitaciones (variación en reporte de AEs, indirectitud) discutidas.                                               |

**Valoración global:** Buena, no detallan los supuestos.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)               |        |                                                                                   |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|-----------------------------------------------------------------------------------|
| Guo 2025 — <i>De novo</i> patients with high-volume metastatic hormone-sensitive prostate cancer can benefit from the addition of docetaxel to triplet therapy: Network-analysis and systematic Review (8) |        |                                                                                   |
| Criterio                                                                                                                                                                                                   | KC     |                                                                                   |
|                                                                                                                                                                                                            | Juicio | Justificación                                                                     |
| 1. ¿Pregunta a priori?                                                                                                                                                                                     | Sí     | Objetivo claro (comparar ARPIs/terapias en mHSPC; OS/PFS).                        |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                                  | Sí     | Justifica NMA por múltiples alternativas y falta de ensayos directos exhaustivos. |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                                 | Sí     | Comparador común (ADT/SOC) descrito dentro de la red.                             |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                           | Sí     | Cumple PRISMA-NMA; proceso de búsqueda y selección informado.                     |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                             | Sí     | Criterios predefinidos                                                            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                                  | Sí     | Reporte de red, geometría y estimaciones por desenlace/subgrupos.                 |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                               | Sí     | Se evalúa coherencia/consistencia y heterogeneidad; ranking bayesiano             |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                                  | Sí     | Modelo bayesiano detallado; herramientas y sensibilidad descritas.                |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                   | Sí     | Limitaciones metodológicas y clínicas discutidas.                                 |

**Valoración global: Alta**, muy sólido en método y reporte PRISMA-NMA.



| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)                                 |         |                                                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|------------------------------------------------------------------------------------------------------------------|
| Aprikian et al.2025 - Meta-analysis to evaluate the comparative effectiveness of enzalutamide and abiraterone acetate for first-line treatment of metastatic castration-resistant prostate cancer in real-world settings (9) |         |                                                                                                                  |
| Criterio                                                                                                                                                                                                                     | KC      |                                                                                                                  |
|                                                                                                                                                                                                                              | Juicio  | Justificación                                                                                                    |
| 1. ¿Pregunta a priori?                                                                                                                                                                                                       | Sí      | Formulada (OS como desenlace principal). Hipótesis explícita.                                                    |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                                                    | Parcial | Se centra en estudios observacionales con comparaciones directas en RWE; la justificación de indirecta es débil. |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                                                   | Parcial | Limitada, solo abiraterona vs enzalutamida en primera línea. No discute comparador común alterno.                |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                                             | Sí      | Cumple PRISMA-NMA; proceso de búsqueda y selección informado.                                                    |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                                               | Sí      | Criterios predefinidos                                                                                           |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                                                    | Parcial | Solo OS con HR ajustados fue metaanalizable; faltaron gráficos de red y comparaciones múltiples.                 |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                                                 | Parcial | Solo sensibilidad en OS, pero no discute transitividad o consistencia.                                           |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                                                    | Parcial | Adecuadas (modelos fijos/aleatorio, sensibilidad). No presenta el código ni comparaciones indirectas ajustadas.  |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                                     | Sí      | Limitaciones metodológicas y clínicas discutidas.                                                                |

**Valoración global: Regular**, comparaciones indirectas no se hicieron con rigurosidad metodológica.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)          |        |                                                                                                       |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|-------------------------------------------------------------------------------------------------------|
| Wang 2024 - Efficacy and safety evaluation of androgen deprivation therapy-based combinations for metastatic castration-sensitive prostate cancer: a systematic review and network meta-analysis (10) |        |                                                                                                       |
| Criterio                                                                                                                                                                                              | KC     |                                                                                                       |
|                                                                                                                                                                                                       | Juicio | Justificación                                                                                         |
| 1. ¿Pregunta a priori?                                                                                                                                                                                | Sí     | Formulada y registro en prospero                                                                      |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                             | Si     | Justifica la necesidad de NMA por ausencia de comparaciones head-to-head completas..                  |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                            | Si     | Bien justificada                                                                                      |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                      | Sí     | Cumple PRISMA-NMA; proceso de búsqueda y selección informado.                                         |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                        | Sí     | Criterios predefinidos                                                                                |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                             | Si     | Con red de 15 tratamientos, gráficos, estimaciones individuales y en red.                             |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                          | Si     | Aborda todos los aspectos metodológicos de una red                                                    |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                             | Si     | Si, con modelo bayesiano, MCMC, comparaciones indirectas ajustadas, detalles técnicos y sensibilidad. |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                              | Sí     | Limitaciones metodológicas y clínicas discutidas.                                                     |

**Valoración global: Alta**, con rigurosidad metodológica y discutidas muy bien las limitaciones.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)                                                       |         |                                                                                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|------------------------------------------------------------------------------------------|
| Dai 2024 – a Meta-Analysis and Meta-Regression of the Efficacy, Toxicity, and Quality of Life Outcomes Following Prostate-Specific Membrane Antigen Radioligand Therapy Utilising Lutetium-177 and Actinium-225 in Metastatic Prostate Cancer (11) |         |                                                                                          |
| Criterio                                                                                                                                                                                                                                           | KC      |                                                                                          |
|                                                                                                                                                                                                                                                    | Juicio  | Justificación                                                                            |
| 1. ¿Pregunta a priori?                                                                                                                                                                                                                             | Sí      | Formulada y registro en prospero                                                         |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                                                                          | Parcial | Justifica la necesidad de NMA pero no deja en claro el supuesto.                         |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                                                                         | Si      | Bien justificada                                                                         |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                                                                   | Sí      | Cumple PRISMA-NMA; proceso de búsqueda y selección informado.                            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                                                                     | Sí      | Criterios predefinidos                                                                   |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                                                                          | Parcial | Incluye datos relevantes, pero no todos.                                                 |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                                                                       | Parcial | Analiza heterogeneidad con meta-regresión, pero no la consistencia ni transitividad.     |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                                                                          | Si      | Si, con modelo bayesiano, comparaciones indirectas ajustadas, pero no publica el código. |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                                                           | Sí      | Limitaciones metodológicas y clínicas discutidas.                                        |

**Valoración global: Alta**, con rigurosidad metodológica y discutidas muy bien las limitaciones.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |              |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|---------------|
| Menges et al 2022 - Treatments for Metastatic Hormone-sensitive Prostate Cancer: Systematic Review, Network Meta-analysis, and Benefit-harm assessment                                       |              |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí           | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Si           | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Si           | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí           | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí           | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Si           | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Si           | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Si           | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí           | NR            |

**Valoración global: Alta,** <sup>a</sup> El estudio contó con un protocolo adecuado, hubo una exhaustiva búsqueda de información, se valoró la calidad de los estudios y se previeron todos los análisis de manera adecuada, la información se entregó bien analizada y se tuvieron en cuenta las limitaciones en el análisis.

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)                     |                                         |               |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|---------------|
| Estudio: Kumar et al. (2020) Comparative efficacy of apalutamide darolutamide and enzalutamide for treatment of non-metastatic castrate-resistant prostate cancer: A systematic review and network meta-analysis |                                         |               |
| Criterio                                                                                                                                                                                                         | KC<br>Juicio                            | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                                           | Probablemente si                        | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                                        | si                                      | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                                       | Si                                      | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                                 | Mas o menos                             | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                                   | Si                                      | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                                        | Posiblemente si pero no hay informacion | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                                     | No                                      | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                                        | Posiblemente si                         | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                         | no                                      | NR            |

**Valoración global: baja**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |                                       |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|---------------|
| Estudio: Hird et al. (2020) A Systematic Review and Network Meta-analysis of Novel Androgen Receptor Inhibitors in Non-metastatic Castration-resistant Prostate Cancer                       |                                       |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio                          | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | no                                    | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | no                                    | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Si                                    | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             |                                       | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Si (Pero tiene riesgos metodológicos) | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Probablemente si                      | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | si                                    | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | No                                    | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Si                                    | NR            |

**Valoración global: baja.**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |                  |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|---------------|
| Estudio: Huang et al. (2024) Efficacy and safety of PARP inhibitors in the treatment of prostatic cancer: a systematic review and network meta-analysis                                      |                  |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio     | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Si               | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | No               | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | SI               | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Si               | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Probablemente si | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | SI               | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Parcialmente     | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Si               | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | NO               | NR            |

**Valoración global: baja**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |                  |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|---------------|
| Estudio: Matsukawa et al. (2025) An Updated Systematic Review and Network Meta-Analysis of First-Line Triplet vs. Doublet Therapies for Metastatic Hormone-Sensitive Prostate Cancer         |                  |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio     | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Si               | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | si               | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Si               | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Si               | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Si               | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Probablemente si | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | No               | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | si               | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | no               | NR            |

**Valoración global: baja**



| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |                  |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|---------------|
| Estudio: Parra et al. (2024) Tratamiento del cáncer de próstata no metastásico resistente a la castración: una revisión sistemática y un metaanálisis                                        |                  |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio     | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Si               | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    |                  | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | si               | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Si               | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Si               | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Si               | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Probablemente si | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    |                  | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Si               | NR            |

**Valoración global: alta**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |                 |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|---------------|
| Estudio: Wang et al. (2024) Network meta-analysis of combination strategies in metastatic hormone-sensitive prostate cancer                                                                  |                 |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio    | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Posiblemente si | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | si              | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Si              | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Parcialmente    | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Si              | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Si              | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | no              | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | no              | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | parcialmente    | NR            |

**Valoración global: baja**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |                                           |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|---------------|
| Estudio: Xiao et al. (2024) Efficacy and safety of androgen receptor inhibitors for treatment of advanced prostate cancer: A systematic review and network meta-analysis (REF)               |                                           |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio                              | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | No hay informacion                        | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Si                                        | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Si                                        | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | SI                                        | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Si, pero no se sabe cuando los definieron | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Probablemente si                          | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Si                                        | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    |                                           | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Si                                        | NR            |

**Valoración global: moderada.**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |              |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|---------------|
| Estudio: Zhu et al. (2024) The efficacy and safety of PARP inhibitors in mCRPC with HRR mutation in second-line treatment: a systematic review and bayesian network meta-analysis            |              |               |
| Criterio                                                                                                                                                                                     | KC<br>Juicio | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Si           | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | si           | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Si           | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Si           | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Si           | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Si           | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Si           | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | si           | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | si           | NR            |

**Valoración global: alta.**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------------------------------------------------------|
| Estudio: Wang 2021 - Comparison of Systemic Treatments for Metastatic Castration-Sensitive Prostate Cancer A Systematic Review and Network Meta-analysis                                     |           |                                                                     |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                     |
|                                                                                                                                                                                              | Juicio    | Justificación                                                       |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Presenta una pregunta adecuada y registrada previamente             |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | La justificación de las comparaciones es clara y adecuada.          |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | La red usa Placebo/ no tratamiento como comparador (es TPA)         |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | Realizaron una búsqueda en bases de datos extensiva.                |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | Sí, lo presentan en la metodología y en el registro de la revisión. |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Presentan una tabla de resultados adecuada.                         |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Realizaron pruebas para evaluar supuestos del MA y del MAR.         |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Realizaron un MAR de tipo bayesiano.                                |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Se presenta de forma extensiva en la discusión.                     |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------------------------------------------------------|
| Estudio: Wang 2021 - Comparison of Systemic Treatments for Metastatic Castration-Sensitive Prostate Cancer A Systematic Review and Network Meta-analysis                                     |           |                                                                     |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                     |
|                                                                                                                                                                                              | Juicio    | Justificación                                                       |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Presenta una pregunta adecuada y registrada previamente             |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | La justificación de las comparaciones es clara y adecuada.          |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | La red usa Placebo/ no tratamiento como comparador (es TPA)         |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | Realizaron una búsqueda en bases de datos extensiva.                |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | Sí, lo presentan en la metodología y en el registro de la revisión. |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Presentan una tabla de resultados adecuada.                         |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Realizaron pruebas para evaluar supuestos del MA y del MAR.         |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Realizaron un MAR de tipo bayesiano.                                |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Se presenta de forma extensiva en la discusión.                     |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)                |           |                                                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|--------------------------------------------------------------------------|
| Estudio: Jiang 2025- Comparative therapeutic efficacy and safety of first-line and second-line therapies for metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis |           |                                                                          |
| Criterio                                                                                                                                                                                                    | Evaluador |                                                                          |
|                                                                                                                                                                                                             | Juicio    | Justificación                                                            |
| 1. ¿Pregunta a priori?                                                                                                                                                                                      | Sí        | Presenta una pregunta clara y presentada en el protocolo en PROSPERO     |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                                   | Sí        | La justificación de la comparación es adecuada                           |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                                  | Sí        | Las redes usan Placebo para la evaluación.                               |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                            | Sí        | Presentaron una búsqueda adecuada.                                       |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                              | Sí        | Sí, lo presentan en la metodología y en el registro de la revisión.      |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                                   | Sí        | Presentan una tabla de resultados adecuada.                              |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                                | Sí        | Realizaron pruebas para evaluar supuestos del MA y del MAR.              |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                                   | Sí        | Realizaron un MAR de tipo bayesiano con técnicas estadísticas adecuadas. |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                    | Sí        | Se presenta de forma extensiva en la discusión.                          |

**Valoración global: Alta**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|--------------------------------------------------------------------------|
| Estudio: Ai 2024 - Comparative effectiveness of first-line systemic treatments for metastatic castration-resistant prostate cancer: a systematic review and network meta-analysis            |           |                                                                          |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                          |
|                                                                                                                                                                                              | Juicio    | Justificación                                                            |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Presenta una pregunta clara y presentada en el protocolo en PROSPERO     |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | La justificación de la comparación es adecuada                           |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | Las redes usan Placebo para la evaluación.                               |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | Presentaron una búsqueda adecuada.                                       |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | No, los criterios son vagos y dan lugar a confusiones.                   |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | No        | La tabla carece de resultados de intervenciones.                         |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Realizaron pruebas para evaluar supuestos del MA y del MAR.              |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Realizaron un MAR de tipo bayesiano con técnicas estadísticas adecuadas. |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Se presenta de forma extensiva en la discusión.                          |

Valoración global: Baja



| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                          |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|--------------------------------------------------------------------------|
| Estudio: Chen 2021 - Comparison of Systemic Treatments for Metastatic Castration-Resistant Prostate Cancer After Docetaxel Failure: A Systematic Review and Network Meta-analysis            |           |                                                                          |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                          |
|                                                                                                                                                                                              | Juicio    | Justificación                                                            |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Presenta una pregunta clara y presentada en el protocolo en PROSPERO     |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | La justificación de la comparación es adecuada                           |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | Las redes usan Placebo para la evaluación.                               |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | Presentaron una búsqueda adecuada.                                       |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | Sí, lo presentan en la metodología y en el registro de la revisión.      |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Presentan una tabla de resultados adecuada.                              |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Realizaron pruebas para evaluar supuestos del MA y del MAR.              |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Realizaron un MAR de tipo bayesiano con técnicas estadísticas adecuadas. |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Se presenta de forma extensiva en la discusión.                          |

**Valoración global: Alta**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------|
| Estudio: Chen 2021 - Comparison of Systemic Treatments for Metastatic Castration-Resistant Prostate Cancer After Docetaxel Failure: A Systematic Review and Network Meta-analysis            |           |               |
| Criterio                                                                                                                                                                                     | Evaluador |               |
|                                                                                                                                                                                              | Juicio    | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | NR            |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)                                    |           |                                           |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-------------------------------------------|
| Estudio: Xiong 2024 - Second-line treatment options in metastatic castration-resistant prostate cancer after progression on first-line androgen-receptor targeting therapies: A systematic review and Bayesian network analysis |           |                                           |
| Criterio                                                                                                                                                                                                                        | Evaluador |                                           |
|                                                                                                                                                                                                                                 | Juicio    | Justificación                             |
| 1. ¿Pregunta a priori?                                                                                                                                                                                                          | Sí        | NR                                        |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                                                       | Sí        | NR                                        |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                                                      | Sí        | NR                                        |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                                                | No        | No utilizaron suficientes bases de datos. |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                                                  | Sí        | NR                                        |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                                                       | Sí        | NR                                        |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                                                    | Sí        | NR                                        |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                                                       | Sí        | NR                                        |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                                        | Sí        | NR                                        |

Valoración global: Moderada

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG)                           |           |               |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------|
| Estudio: Wang 2020 - Comparative Efficacy of Combined Radiotherapy, Systemic Therapy, and Androgen Deprivation Therapy for Metastatic Hormone-Sensitive Prostate Cancer: A Network Meta-Analysis and Systematic Review |           |               |
| Criterio                                                                                                                                                                                                               | Evaluador |               |
|                                                                                                                                                                                                                        | Juicio    | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                                                 | Sí        | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                                              | Sí        | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                                             | Sí        | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                                                       | Sí        | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                                                         | Sí        | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                                              | Sí        | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                                           | Sí        | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                                              | Sí        | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                                               | Sí        | NR            |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------|
| Estudio: Zhu 2024 - The efficacy and safety of PARP inhibitors in mCRPC with HRR mutation in second-line treatment: a systematic review and bayesian network meta-analysis                   |           |               |
| Criterio                                                                                                                                                                                     | Evaluable |               |
|                                                                                                                                                                                              | Juicio    | Justificación |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | NR            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | NR            |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | NR            |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | NR            |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | NR            |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | NR            |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | NR            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | NR            |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | NR            |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-------------------------------------------------------------------------------------|
| Estudio: Mandel 2024 - Triplet or Doublet Therapy for Metastatic Hormone-sensitive Prostate Cancer: A Systematic Review and Network Meta-analysis                                            |           |                                                                                     |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                                     |
|                                                                                                                                                                                              | Juicio    | Justificación                                                                       |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Pregunta PICO y objetivos pre-especificados; enfoque en doblete/triplete fase III.  |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | Existen comparaciones no directamente evaluadas entre regímenes; NMA es pertinente. |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | ADT±docetaxel/ARAT como nodos puente clínicamente relevantes.                       |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | PubMed/Embase/CENTRAL/ClinicalTrials/actas; flujo PRISMA..                          |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | ECA fase III en mHSPC; exclusiones claras.                                          |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Red, tablas por ensayo, HR e IC95%; transparencia alta.                             |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Heterogeneidad, consistencia y sensibilidad reportadas.                             |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | NMA frecuentista (netmeta), efectos aleatorios; detalles de $\tau^2/I^2$ .          |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Diferencias de población y madurez de datos discutidas.                             |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------------------------------------------|
| Estudio: Sathianathen 2023- Comparison of Systemic Treatments for Metastatic Castration-Sensitive Prostate Cancer A Systematic Review and Network Meta-analysis                              |           |                                                         |
| Criterio                                                                                                                                                                                     | Evaluador |                                                         |
|                                                                                                                                                                                              | Juicio    | Justificación                                           |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Pregunta PICO y outcomes predefinidos.                  |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | NMA necesaria para comparar regímenes sin head-to-head. |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | ADT±ARAT/docetaxel como nodo común.                     |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | Búsqueda exhaustiva (bases + congresos) con PRISMA.     |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | Inclusión/exclusión ECA fase III claramente descrita.   |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Reporte completo (red, HR/IC, SUCRA)                    |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Consistencia/convergencia (PSRF) y sensibilidad.        |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Bayesiano (gemtc); especificación del modelo adecuada.  |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Limitaciones y supuestos discutidos.                    |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                        |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|------------------------------------------------------------------------|
| Estudio: Riaz 2023- First-line Systemic Treatment Options for Metastatic Castration-Sensitive Prostate Cancer A Living Systematic Review and Network Meta-analysis                           |           |                                                                        |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                        |
|                                                                                                                                                                                              | Juicio    | Justificación                                                          |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Pregunta a priori y protocolo OSF/registro.                            |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | NMA justificada; comparaciones no directas entre tripletes y dobletes. |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | ADT±docetaxel/ARAT como comparador común.                              |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | MEDLINE/Embase desde inicio + actualización automática; PRISMA.        |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | Criterios definidos (fase III, primera línea).                         |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Datos completos (HR, P-scores, subgrupos).                             |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Supuestos evaluados; no todas las pruebas formales en red..            |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Frecuentista (netmeta); par-wise random y red fija justificados.       |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Limitaciones del modelo fijo y mezcla poblacional discutidas           |

**Valoración global: Alta**



| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------------------------------------------|
| Estudio: Shing (Zheng) 2022- First-line Therapy for Metastatic Castration-Sensitive Prostate Cancer: A Network Meta-Analysis                                                                 |           |                                                         |
| Criterio                                                                                                                                                                                     | Evaluador |                                                         |
|                                                                                                                                                                                              | Juicio    | Justificación                                           |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Pregunta PICO definida.                                 |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | La justificación de la comparación es adecuada          |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | ADT±docetaxel/ARAT como comparador común.               |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | úsqueda amplia (≥6 fuentes) y PRISMA.                   |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | Criterios claros a priori.                              |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Reporte completo (red, HR, P-scores).                   |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Heterogeneidad baja; inconsistencia formal no evaluada. |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Frecuentista (R), modelos fijo/aleatorio descritos.     |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Limitaciones de red y datos discutidas.                 |

**Valoración global: Baja**

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                                                           |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------|
| Estudio: Chen 2020 - Comparative efficacy and safety of systemic therapies for metastatic hormone-sensitive prostate cancer: A network meta-analysis                                         |           |                                                                                                           |
| Criterio                                                                                                                                                                                     | Evaluable |                                                                                                           |
|                                                                                                                                                                                              | Juicio    | Justificación                                                                                             |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Protocolo PROSPERO (CRD42019132967) y objetivos definidos.                                                |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | Comparar múltiples combinaciones sin comparaciones directas completas.                                    |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | Red anclada en ADT; coherencia clínica de nodos.                                                          |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | MEDLINE/EMBASE/CENTRAL/ClinicalTrials.gov, sin restricción de idioma; PRISMA.                             |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | ECAs con OS/FFS/AEs; definiciones y filtros claros.                                                       |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | PRISMA, red, características, HR/IC/CrI y tabla de AEs ≥G3.                                               |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Heterogeneidad ( $I^2/\chi^2$ ), consistencia y análisis de sensibilidad; subgrupos por volumen/visceral. |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Bayes (gemtc) con SUCRA; modelos fijo/aleatorio; criterios de convergencia.                               |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Diferencias entre ensayos y riesgos de AEs mayores con ciertos regímenes analizados.                      |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                                                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------------------------------------------------------------------------------------|
| Estudio: Jian 2023- Comparison of Combination Therapies in Metastatic Hormone-sensitive Prostate Cancer: A Bayesian Network Meta-analysis                                                    |           |                                                                                                   |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                                                   |
|                                                                                                                                                                                              | Juicio    | Justificación                                                                                     |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Protocolo registrado en PROSPERO y objetivo PICO explícito.                                       |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | Múltiples regímenes sin comparaciones directas completas; NMA necesaria.                          |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | Red con ADT ( $\pm$ SNA/docetaxel/ARTA) como nodo puente clínicamente válido.                     |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | Sí        | PubMed, Embase, CENTRAL, registros y congresos; PRISMA-NMA.                                       |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | ECA con OS/rPFS/AE; exclusiones claras.                                                           |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Red, tablas de ensayos, HR/CrI y AEs (arm-based) completamente presentados.                       |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | Sí        | Homogeneidad ( $I^2$ ), consistencia y transitividad evaluadas; exclusión de alta heterogeneidad. |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Bayes (gemtc) fijo/aleatorio para eficacia; frecuentista para AEs; SUCRA; R 4.1.2.                |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Incertidumbre de bucles cerrados por subgrupos y madurez de datos.                                |

Valoración global: Alta

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                                                      |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|------------------------------------------------------------------------------------------------------|
| Estudio: Hoeh 2024- Triplet or Doublet Therapy in Metastatic Hormone-sensitive Prostate Cancer Patients: An Updated Network Meta-analysis Including ARANOTE Data                             |           |                                                                                                      |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                                                      |
|                                                                                                                                                                                              | Juicio    | Justificación                                                                                        |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Objetivo de embedder ARANOTE dentro del panorama terapéutico, declarado desde inicio.                |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | Diferencias de diseño y ausencia de head-to-head, NMA apropiada.                                     |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | Referencia ADT (y análisis con ARAT+ADT agrupado).                                                   |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | No        | Se apoya en metodología previa y datos ESMO 2024; no detalla búsqueda integral en esta carta.        |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | 11 ECA especificados; foco en PFS/OS                                                                 |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Forest plots, red de tratamientos y HR/IC; OS de ARANOTE señalado como inmaduro.                     |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | No        | Efectos aleatorios y estratificación por volumen; no se informan pruebas formales de inconsistencia. |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Frecuentista con efectos aleatorios; R; enfoque coherente con trabajo previo.                        |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Seguimiento corto de ARANOTE y cautela en OS explícitamente discutidos.                              |

Valoración global: Moderada

| Valoración de la calidad metodológica de revisiones sistemáticas con metanálisis de comparaciones indirectas o metaanálisis en red. Herramienta adaptada al español a partir de: (1) (IQWiG) |           |                                                                                                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|---------------------------------------------------------------------------------------------------------|
| Estudio: Hoeh 2023 Triplet or Doublet Therapy in Metastatic Hormone-sensitive Prostate Cancer: Updated Network Meta-analysis Stratified by Disease Volume                                    |           |                                                                                                         |
| Criterio                                                                                                                                                                                     | Evaluador |                                                                                                         |
|                                                                                                                                                                                              | Juicio    | Justificación                                                                                           |
| 1. ¿Pregunta a priori?                                                                                                                                                                       | Sí        | Actualizar OS por volumen (low/high) en mHSPC.                                                          |
| 2. ¿Justifica usar comparación indirecta?                                                                                                                                                    | Sí        | No hay ECAs triplete vs ARAT+ADT; NMA necesaria.                                                        |
| 3. ¿Justifica comparador común vs directa?                                                                                                                                                   | Sí        | Referencia ADT y, en análisis clave, ARAT+ADT agrupado.                                                 |
| 4. ¿Búsqueda sistemática y exhaustiva, descrita?                                                                                                                                             | No        | Resultados de 10 ECAs hasta ASCO-GU 2023" siguiendo metodología previa; sin detalle de estrategia/bases |
| 5. ¿Criterios de inclusión/exclusión predefinidos y descritos?                                                                                                                               | Sí        | ECAs de dobletes/tripletes; volumen según CHAARTED.                                                     |
| 6. ¿Reporte completo de datos relevantes?                                                                                                                                                    | Sí        | Forest plots, red y rankings (P-score)                                                                  |
| 7. ¿Supuestos clave investigados y tratados?                                                                                                                                                 | No        | Modelos de efectos aleatorios; no se reporta inconsistencia formal.                                     |
| 8. ¿Herramientas estadísticas adecuadas y bien descritas?                                                                                                                                    | Sí        | Frecuentista (R 3.4.3) con efectos aleatorios.                                                          |
| 9. ¿Limitaciones descritas y discutidas?                                                                                                                                                     | Sí        | Diferencias de seguimiento y ausencia de head-to-head discutidas.                                       |

**Valoración global: Moderada**

## Anexo I. Extracción de información de seguridad y efectividad

Tabla I-1. Matriz de extracción de información para la pregunta 1.

| Auto<br>r y<br>Año  | Fuen<br>te                  | Nomb<br>re          | Tipo de<br>Estudio                                                                         | Diagnóstic<br>o                                                                                                                                                                                                                | Edad                                                       | N por brazo<br>(n/n)                                         | Intervenció<br>n                                                                                                             | TPA<br>específico                                                          | Antiandrógeno<br>(anti-flare)                            | Compara<br>dor                                                             | Supervive<br>ncia<br>global<br>(OS)                                                                   | Supervive<br>ncia libre<br>de<br>progresió<br>n (PFS)                                                                                                                  | Tasa<br>de<br>respue<br>sta<br>objetiv<br>a<br>(ORR) | Calida<br>d de<br>vida<br>(HRQo<br>L)                                                                                    | Eventos<br>adversos<br>totales                                                                                    | EA graves<br>(SAEs)                                                                        | Curvas de<br>supervive<br>ncia                                                                                                                                     |
|---------------------|-----------------------------|---------------------|--------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|--------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sarg<br>os,<br>2020 | Estudi<br>o<br>prima<br>rio | TAP<br>32           | ECA Fase<br>3,<br>Aleatoriz<br>ado,<br>Abierto                                             | Adenocarcin<br>oma de<br>próstata<br>localmente<br>avanzado<br>(T3–T4). No<br>metástasis<br>(N0, M0).<br>PSA<br>mediana<br>26.8<br>ng/mL;<br>Gleason ≥ 7<br>en 51.3%.                                                          | Media:<br>70.6<br>años<br>(DE<br>5.6).                     | ADT+EBRT:<br>133 / ADT<br>solo: 130.                         | Leuprorelin<br>(3 años) +<br>Flutamida (1<br>mes) + EBRT<br>(Dosis<br>mediana 70<br>Gy).                                     | Leuprorelin<br>11.25 mg<br>(subcutáneo)                                    | Flutamida oral (750<br>mg/día, durante el<br>primer mes) | Leuproreli<br>n +<br>Flutamida<br>(3 años<br>de TPA).                      | 8 años:<br>65%<br>(ADT+EBR<br>T) vs 57%<br>(ADT sola).<br>(No fue<br>significativ<br>o, P =<br>0.43). | 8 años<br>PFS: 48%<br>(ADT+EBR<br>T) vs 7%<br>(ADT sola).<br>HR 0.27<br>(95% CI<br>0.17–<br>0.39). MFS<br>fue<br>comparable<br>entre<br>ambos<br>brazos (P =<br>0.88). | No<br>evaluad<br>o                                   | No<br>evaluad<br>o                                                                                                       | Toxicidad<br>aguda fue<br>significativa<br>mente más<br>frecuente en<br>ADT+EBRT<br>(26%) vs<br>ADT sola<br>(2%). | Eventos<br>Adversos<br>Graves<br>(SAEs) en<br>el brazo<br>ADT+EBRT<br>vs 8 en<br>ADT solo. | Superviven<br>cia Libre de<br>Progresión<br>(PFS), la<br>Superviven<br>cia Global<br>(OS) y la<br>Superviven<br>cia Libre de<br>Progresión<br>Bioquímica<br>(BPFS) |
| Lee,<br>2024        | Estudi<br>o<br>prima<br>rio | COHO<br>RT<br>trial | ECA Fase<br>3,<br>Aleatoriz<br>ado,<br>Multicén<br>trico<br>(Análisis<br>Per-<br>protocol) | Cáncer de<br>próstata<br>clínicament<br>e<br>ganglionar<br>positivo<br>(N+) y no<br>metastásico<br>(M0). Todos<br>T3 o T4;<br>84.7%<br>Gleason ≥<br>8. Los<br>ganglios<br>debían<br>haber<br>respondido<br>a TPA<br>neoadyuvan | Media<br>na: 70<br>años<br>(Rang<br>o: 49–<br>83<br>años). | ADT+RT: 28 /<br>ADT solo: 31<br>(Análisis per-<br>protocol). | TPA +<br>bicalutamida<br>(al menos 2<br>años). RT<br>pélvica con<br>IMRT (Dosis<br>principal: 70<br>Gy en 28<br>fracciones). | Leuprolide<br>(59.3%),<br>triptorelin<br>(35.6%), o<br>goserelin<br>(5.1%) | Bicalutamida                                             | TPA<br>(agonista<br>GnRH +<br>bicalutam<br>ida) por<br>al menos<br>2 años. | No<br>evaluado                                                                                        | No<br>evaluado                                                                                                                                                         | No<br>evaluad<br>o                                   | EPIC<br>sin<br>diferenc<br>ias<br>entre<br>dominio<br>s<br>(urinari<br>o, p =<br>0.202;<br>intestin<br>al, p =<br>0.050) | Mayor<br>incidencia de<br>eventos<br>adversos<br>(AEs).                                                           | Ningún<br>SAEs<br>reportado                                                                | No incluye                                                                                                                                                         |

| Auto<br>r y<br>Año | Fuen<br>te                  | Nomb<br>re         | Tipo de<br>Estudio        | Diagnóstic<br>o                                                                                                                                          | Edad                                                                                                                            | N por brazo<br>(n/n)           | Intervenció<br>n                                                                              | TPA<br>específico                     | Antiandrógeno<br>(anti-flare)                                         | Compara<br>dor                                        | Supervive<br>ncia<br>global<br>(OS)                                                                     | Supervive<br>ncia libre<br>de<br>progresió<br>n (PFS)                                                                      | Tasa de<br>respue<br>sta<br>objetiv<br>a<br>(ORR) | Calida<br>d de<br>vida<br>(HRQo<br>L) | Eventos<br>adversos<br>totales                                                                             | EA graves<br>(SAEs)                                                                                                                                   | Curvas de<br>supervive<br>ncia                                                                                                                |
|--------------------|-----------------------------|--------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|--------------------------------|-----------------------------------------------------------------------------------------------|---------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------|---------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------------------|------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
|                    |                             |                    |                           | te (2-3<br>meses).                                                                                                                                       |                                                                                                                                 |                                |                                                                                               |                                       |                                                                       |                                                       |                                                                                                         |                                                                                                                            |                                                   |                                       |                                                                                                            |                                                                                                                                                       |                                                                                                                                               |
| Bolla,<br>2010     | Estudi<br>o<br>prima<br>rio | EORT<br>C<br>22863 | ECA Fase<br>3,<br>Abierto | Cáncer de<br>próstata<br>con alto<br>riesgo<br>metastásico<br>(T1-2 G3 o<br>T3-4 de<br>cualquier<br>grado).<br>90% T3-<br>T4. No<br>metastásico<br>(M0). | Media<br>na: 70<br>años<br>(RIC<br>65-<br>75)<br>para<br>RT<br>sola;<br>71<br>años<br>(RIC<br>67-<br>75)<br>para<br>RT+TP<br>A. | RT+TPA: 207<br>/ RT sola: 208. | LHRH<br>agonista/gos<br>erelin +<br>antiandrógen<br>o, durante 3<br>años. Dosis<br>RT: 70 Gy. | Goserelin<br>acetate s.c.<br>cada mes | Ciproterona acetato<br>(50 mg oral, 3<br>veces/día, durante 1<br>mes) | Radioter<br>apia sola<br>(RT).<br>Dosis RT:<br>70 Gy. | HR 0.60<br>(95% CI<br>0.45-<br>0.80).<br>10 años:<br>58.1%<br>(Combinad<br>o) vs<br>39.8% (RT<br>sola). | HR 0.42<br>(95% CI<br>0.33-<br>0.55).<br>10 años<br>Clinical<br>DFS:<br>47.7%<br>(Combinad<br>o) vs<br>22.7% (RT<br>sola). | No<br>evaluad<br>o                                | No<br>evaluad<br>o                    | Incidencia de<br>muertes por<br>enfermedad<br>cardiovascula<br>r: 22<br>(Combinado)<br>vs 17 (RT<br>sola). | No hubo<br>diferencia<br>significativ<br>a en la<br>mortalidad<br>cardiovascu<br>lar. Dos<br>fracturas<br>reportadas<br>en el brazo<br>combinado<br>. | Superviven<br>cia Libre de<br>Progresión<br>Clínica<br>(Clinical<br>disease-<br>free<br>survival) y<br>la<br>Superviven<br>cia Global<br>(OS) |

Tabla I-2. Matriz de extracción de información para la pregunta 2.

| Estudio     | Autor       | Año  | Tipo de<br>estudi<br>o | Tratamient<br>o        | N<br>por<br>braz<br>o | Edad           | Score<br>Gleaso<br>n | PSA<br>median<br>o | Metástas<br>is<br>visceral | HR de<br>Supervivenc<br>ia global<br>(IC95) | Numer<br>o de<br>evento<br>s OS | HR PSA<br>PFS<br>(IC95) | Numero<br>de<br>eventos<br>PFS | HR<br>Supervivenc<br>ia libre de<br>progresion<br>radiologica | Numero<br>de<br>eventos<br>RPFS | HR<br>Metastas<br>is free<br>survival | Eventos<br>Metastas<br>is | Eventos<br>adverso<br>s<br>graves | Cualqui<br>er EA |
|-------------|-------------|------|------------------------|------------------------|-----------------------|----------------|----------------------|--------------------|----------------------------|---------------------------------------------|---------------------------------|-------------------------|--------------------------------|---------------------------------------------------------------|---------------------------------|---------------------------------------|---------------------------|-----------------------------------|------------------|
| PROSPE<br>R | Hussai<br>n | 2018 | Ensay<br>o<br>clínico  | Enzalutami<br>da + TPA | 933                   | 74 (50-<br>95) | NR                   | 11.1               | NA                         | 0,73 (0.61-<br>0.89)                        | 103                             | 0,07<br>(0,05-<br>0,08) | 208                            | NR                                                            | 744                             | 0,29<br>(0,24-<br>0,35)               | 219                       | 226                               | 808              |
| PROSPE<br>R | Hussai<br>n | 2018 | Ensay<br>o<br>clínico  | Placebo +<br>TPA       | 468                   | 73 (53-<br>92) | NR                   | 10.2               | NA                         | NA                                          | 62                              | NA                      | 324                            |                                                               | 244                             | NA                                    | 228                       | 85                                | 360              |
| SPARTA<br>N | Smith       | 2018 | Ensay<br>o<br>clínico  | Apalutadmi<br>a + TPA  | 806                   | 74 (48-<br>94) | NR                   | 7,78               | NA                         | 0,70 (0,47-<br>1.04)                        | 10                              | 0,06<br>(0,05-<br>0,08) | NR                             |                                                               |                                 | 0,28<br>(0,23-<br>0,35)               | 184                       | 199                               | 775              |

| Estudio | Autor  | Año  | Tipo de estudio | Tratamiento        | N por brazo | Edad       | Score Gleason | PSA mediano | Metástasis visceral | HR de Supervivencia global (IC95) | Número de eventos OS | HR PSA PFS (IC95) | Número de eventos PFS | HR Supervivencia libre de progresión radiológica | Número de eventos RPFS | HR Metástasis free survival | Eventos Metástasis | Eventos adversos graves | Cualquier EA |
|---------|--------|------|-----------------|--------------------|-------------|------------|---------------|-------------|---------------------|-----------------------------------|----------------------|-------------------|-----------------------|--------------------------------------------------|------------------------|-----------------------------|--------------------|-------------------------|--------------|
| SPARTAN | Smith  | 2018 | Ensayo clínico  | Placebo + TPA      | 401         | 74 (52-97) | NR            | 7,96        | NA                  | NA                                | 1                    | NA                | NR                    |                                                  |                        | NA                          | 194                | 92                      | 371          |
| ARAMIS  | Fizazi | 2019 | Ensayo clínico  | Darolutamida + TPA | 55          | 74 (48-95) | NR            | 9           | NA                  | 0,71 (0,50-0,99)                  | 78                   | 0,13 (0,11-0,16)  | 255                   |                                                  |                        | 0,41 (0,34-0,50)            | 221                | 237                     | 794          |
| ARAMIS  | Fizazi | 2019 | Ensayo clínico  | Placebo + TPA      | 554         | 74 (50-92) | NR            | 9,7         | NA                  | NA                                | 58                   | NA                | 258                   |                                                  |                        | NA                          | 216                | 111                     | 426          |
| STRIVE  | Penson | 2016 | Ensayo clínico  | Enzalutamida + TPA | 140         | 72 (46-92) | NR            | 11          | NA                  |                                   |                      | 0,18 (0,10-0,34)  |                       |                                                  |                        |                             |                    | 58                      | 184          |
| STRIVE  | Penson | 2016 | Ensayo clínico  | Bicalutamida + TPA | 138         | 74 (50-91) | NR            | 13,2        | NA                  |                                   |                      | NA                |                       |                                                  |                        |                             |                    | 56                      | 177          |

Tabla I-3. Matriz de extracción de información para la pregunta 3.

| ID_art | Estudio                         | Autor          | Año  | Tipo de estudio                                             | Tratamiento                                                   | N por brazo | Edad                   | Score Gleason                     | PSA mediano                                          | Metástasis visceral | Análisis por subgrupo (Low vs High) | Tratamiento previo                         | HR de Supervivencia global (IC95) | Número de eventos OS | HR PFS (IC95)                                                                 | Número de eventos PFS | Eventos adversos graves                                   |
|--------|---------------------------------|----------------|------|-------------------------------------------------------------|---------------------------------------------------------------|-------------|------------------------|-----------------------------------|------------------------------------------------------|---------------------|-------------------------------------|--------------------------------------------|-----------------------------------|----------------------|-------------------------------------------------------------------------------|-----------------------|-----------------------------------------------------------|
| 1      | Casodex Combination Study Group | Schellhammer P | 1995 | ECA fase III, multicéntrico, doble ciego para antiandrógeno | TPA + Bicalutamida (50 mg/d) + LHRH-A (goserelina/leuprolida) | 404         | Media 70 (rango 43-91) | Pobre 33%, Moderado 50%, Bien 14% | NI (basal elevado en 766/813; reducción mediana 99%) | NI                  | High                                | Exclusión de terapia sistémica previa → No | HR OS 0.97 (95% CI 0.70-1.35)     | 68/404 (17%)         | HR TTF 0.749 (95% CI 0.61-0.92) vs flutamida (PFS no reportado como primario) | 168/404 fallos (42%)  | Retiro por EA: 32/401; diarrea 2, LFT anormales 6, otros  |
| 1      | Casodex Combination Study Group | Schellhammer P | 1995 | ECA fase III, multicéntrico, doble ciego para antiandrógeno | TPA + Flutamida (250 mg TID) + LHRH-A (goserelina/leuprolida) | 409         | Media 70 (rango 42-93) | Pobre 36%, Moderado 49%, Bien 11% | NI (basal elevado; reducción)                        | NI                  | High                                | No                                         | HR OS 1.0 (comparador)            | 73/409 (18%)         | Ref: HR 1.0 (comparador)                                                      | 218/409 fallos (53%)  | Retiro por EA: 56/407; diarrea 25, LFT anormales 8, otros |



| ID_art | Estudio                         | Autor          | Año  | Tipo de estudio                                               | Tratamiento                                                                           | N por brazo | Edad                            | Score Gleason                               | PSA media no                                            | Metástasis visceral | Análisis por subgrupo (Low vs High) | Tratamiento previo               | HR de Supervivencia global (IC95) | Número de eventos OS | HR PFS (IC95)                                      | Numero de eventos PFS   | Eventos adversos graves                                                                              |
|--------|---------------------------------|----------------|------|---------------------------------------------------------------|---------------------------------------------------------------------------------------|-------------|---------------------------------|---------------------------------------------|---------------------------------------------------------|---------------------|-------------------------------------|----------------------------------|-----------------------------------|----------------------|----------------------------------------------------|-------------------------|------------------------------------------------------------------------------------------------------|
|        |                                 |                |      |                                                               |                                                                                       |             |                                 |                                             | media a 99%)                                            |                     |                                     |                                  |                                   |                      |                                                    |                         |                                                                                                      |
| 2      | Casodex Combination Study Group | Schellhammer P | 1996 | ECA fase III, multicéntrico, doble ciego para antiandrogénico | TPA + Bicalutamida (50 mg/d) + LHRH-A (goserelina/leuprolida)                         | 404         | Media 70 (rango similar a 1995) | NI (baseline: pobre/mod/bien diferenciados) | NI (baseline elevado; reducción media a 99% en cohorte) | NI                  | High                                | No (exclusión de terapia previa) | HR OS 0.88 (95% CI 0.69–1.11)     | NI                   | HR TTP 0.90 (95% CI 0.75–1.08; p=0.26)             | 223/404 (55%) progresar | NI                                                                                                   |
| 2      | Casodex Combination Study Group | Schellhammer P | 1996 | ECA fase III, multicéntrico, doble ciego para antiandrogénico | TPA + Flutamida (250 mg TID) + LHRH-A (goserelina/leuprolida)                         | 409         | Media 70 (rango 43–91)          | Pobre 33%, Moderado 50%, Bien 14%           | NI (basal elevado en 766/813; reducción media a 99%)    | NI                  | High                                | No                               | HR OS 1.0 (comparador)            | NI                   | Ref: HR 1.0 (comparador)                           | 235/409 (58%) progresar | NI                                                                                                   |
| 3      | KYUCOG-1401                     | Yokomizo A     | 2024 | ECA fase III, abierto, multicéntrico                          | Degarelix (GnRH antagonista) monoterapia (± adición tardía bicalutamida al progresar) | 100         | Media 74.5 (59–90)              | Gleason ≥8: 91%                             | PSA ≥100 ng/mL en 65%                                   | M1: 78%             | High                                | No                               | HR OS 1.17 (95% CI 0.69–1.96)     | NI                   | HR PSA-PFS 1.40 (95% CI 1.01–1.95; p=0.041) [peor] | NI                      | Inyección sitio 34.3% (1 grave), hiperK+ 52% (3 graves), anemia 88% (3 graves), ↑ALP 69% (14 graves) |
| 3      | KYUCOG-1401                     | Yokomizo A     | 2024 | ECA fase III, abierto, multicéntrico                          | CAB: agonista GnRH (leuprorelina/goserelin) +                                         | 98          | Media 73 (55–89)                | Gleason ≥8: 91.8%                           | PSA ≥100 ng/mL en 64%                                   | M1: 82.7%           | High                                | No                               | HR OS 1.0 (comparador)            | NI                   | Ref: HR 1.0 (comparador)                           | NI                      | Inyección sitio 7.2% (0 graves), anemia 95.8% (5                                                     |

| ID_art | Estudio                         | Autor           | Año  | Tipo de estudio                                             | Tratamiento                                          | N por brazo | Edad             | Score Gleason                             | PSA medio                             | Metástasis visceral                  | Análisis por subgrupo (Low vs High) | Tratamiento previo | HR de Supervivencia global (IC95) | Número de eventos OS | HR PFS (IC95)                          | Número de eventos PFS  | Eventos adversos graves                                                          |
|--------|---------------------------------|-----------------|------|-------------------------------------------------------------|------------------------------------------------------|-------------|------------------|-------------------------------------------|---------------------------------------|--------------------------------------|-------------------------------------|--------------------|-----------------------------------|----------------------|----------------------------------------|------------------------|----------------------------------------------------------------------------------|
|        |                                 |                 |      |                                                             | bicalutamida 80 mg/d                                 |             |                  |                                           |                                       |                                      |                                     |                    |                                   |                      |                                        |                        | graves),<br>↑ALP 81% (18 graves),<br>↑ALT 21% (3 graves)                         |
| 4      | Intergroup 0036                 | Crawford ED     | 1989 | ECA fase III, multicéntrico, doble ciego                    | TPA (leuprolide) + flutamida 250 mg TID              | 303         | Media 69 (44–86) | NI                                        | NI                                    | 66% metástasis óseas, 20% viscerales | High                                | No                 | Mediana OS 35.6 meses             | 149 muertes          | Mediana PFS 16.5 meses                 | 180 progresiones       | Diarrea 13.6% (vs 4.9%), hepatotox 1.8%, ginecomastia 6.7%                       |
| 4      | Intergroup 0036                 | Crawford ED     | 1989 | ECA fase III, multicéntrico, doble ciego                    | TPA (leuprolide) + placebo                           | 300         | Media 68 (46–96) | NI                                        | NI                                    | 66% óseas, 18% viscerales            | High                                | No                 | Mediana OS 28.3 meses             | 149 muertes          | Mediana PFS 13.9 meses                 | 171 progresiones       | Diarrea 4.9%, hepatotox 0.8%, ginecomastia 1.7%                                  |
| 5      | Casodex Combination Study Group | Schellhammer PF | 1997 | ECA fase III, multicéntrico, doble ciego para antiandrógeno | TPA (goserelina o leuprolide) + Bicalutamida 50 mg/d | 404         | Media 70 (43–91) | Gleason pobre 33%, moderado 50%, bien 14% | Reducción PSA mediana a 99% a 3 meses | NI                                   | High                                | No (hormono naive) | HR OS 0.87 (95% CI 0.72–1.05)     | 213 muertes (53%)    | HR TTP 0.93 (95% CI 0.79–1.10; p=0.41) | 287 progresiones (71%) | Diarrea 12% (2 retiros), hematuria 12%, LFT anormales 7%; 41/401 retiros por EA  |
| 5      | Casodex Combination Study Group | Schellhammer PF | 1997 | ECA fase III, multicéntrico, doble ciego para antiandrógeno | TPA (goserelina o Flutamida 250 mg TID               | 409         | Media 70 (42–93) | Gleason pobre 36%, moderado 49%, bien 11% | Reducción PSA mediana a 99% a 3 meses | NI                                   | High                                | No                 | HR OS 1.0 (comparador)            | 235 muertes (57%)    | Ref: HR 1.0 (comparador)               | 296 progresiones (72%) | Diarrea 26% (25 retiros), hematuria 6%, LFT anormales 11%; 66/407 retiros por EA |

| ID_art | Estudio           | Autor          | Año  | Tipo de estudio                                                                  | Tratamiento                                  | N por brazo | Edad               | Score Gleason                     | PSA media no                                                      | Metástasis visceral              | Análisis por subgrupo (Low vs High) | Tratamiento previo            | HR de Supervivencia global (IC95) | Número de eventos OS | HR PFS (IC95)                  | Número de eventos PFS  | Eventos adversos graves                                                                |
|--------|-------------------|----------------|------|----------------------------------------------------------------------------------|----------------------------------------------|-------------|--------------------|-----------------------------------|-------------------------------------------------------------------|----------------------------------|-------------------------------------|-------------------------------|-----------------------------------|----------------------|--------------------------------|------------------------|----------------------------------------------------------------------------------------|
| 6      | CASODEX factorial | Sarosdy MF     | 1998 | ECA fase III, multicéntrico, abierto para LHRH-A, doble ciego para antiandrogéno | Leuprolide 7.5 mg/28d + Bicalutamida 50 mg/d | 136         | Media 70.1 (44–91) | Pobre 17%, moderado 40%, bien 38% | NI                                                                | ≥6 metástasis 39%, viscerales NI | High                                | No                            | NI                                | 67 muertes (49%)     | NI                             | 94 progresiones (69%)  | Hematuria 11%, diarrea 10%, astenia 14%                                                |
| 6      | CASODEX factorial | Sarosdy MF     | 1998 | ECA fase III, multicéntrico                                                      | Leuprolide + Flutamida 250 mg TID            | 137         | Media 70.6 (44–89) | Pobre 13%, moderado 44%, bien 38% | NI                                                                | ≥6 metástasis 34%                | High                                | No                            | NI                                | 88 muertes (64%)     | NI                             | 106 progresiones       | Diarrea 30%, hepatotox 9%, astenia 25%                                                 |
| 6      | CASODEX factorial | Sarosdy MF     | 1998 | ECA fase III, multicéntrico                                                      | Goserelin 3.6 mg/28d + Bicalutamida 50 mg/d  | 268         | Media 69.7 (43–89) | Pobre 13%, moderado 55%, bien 30% | NI                                                                | ≥6 metástasis 39%                | High                                | No                            | NI                                | 146 muertes (54%)    | NI                             | 193 progresiones (72%) | Diarrea 13%, hematuria 12%                                                             |
| 6      | CASODEX factorial | Sarosdy MF     | 1998 | ECA fase III, multicéntrico                                                      | Goserelin + Flutamida 250 mg TID             | 272         | Media 70.3 (42–93) | Pobre 10%, moderado 51%, bien 35% | NI                                                                | ≥6 metástasis 42%                | High                                | No                            | NI                                | 147 muertes (54%)    | NI                             | 190 progresiones (70%) | Diarrea 24%, hepatotox 12%                                                             |
| 7      | JAMA Oncol Trial  | Vaishampayan U | 2021 | ECA fase II, multicéntrico, abierto                                              | ADT + Enzalutamida 160 mg/d                  | 36          | Media 66 (54–86)   | Gleason ≥8: 64%                   | NI (PSA basal mediana no reportada en tabla, pero todos ≥4 ng/mL) | Visceral 3/36 (8%)               | High                                | No (ADT naïve, sin docetaxel) | HR OS 0.31 (95% CI 0.13–0.74)     | 9 muertes            | HR TTP 0.15 (95% CI 0.05–0.47) | 8 progresiones (22%)   | Hipertensión grado 3 en 3 ptes; síncope grado 3 en 2; un caso de convulsión (retirado) |
| 7      | JAMA Oncol Trial  | Vaishampayan U | 2021 | ECA fase II, multicéntrico, abierto                                              | ADT + Bicalutamida 50 mg/d                   | 35          | Media 66 (51–84)   | Gleason ≥8: 49%                   | NI (PSA basal mediana no reportada en                             | Visceral 2/35 (6%)               | High                                | No                            | HR OS 1.0 (comparador)            | 17 muertes           | Ref: HR 1.0 (comparador)       | 12 progresiones (34%)  | Hipertensión grado 3 en 1 pt; fatiga grado 3 en 2; sin                                 |

| ID_art | Estudio  | Autor        | Año  | Tipo de estudio                          | Tratamiento                                                                                          | N por brazo | Edad                      | Score Gleason           | PSA medio                         | Metástasis visceral | Análisis por subgrupo (Low vs High) | Tratamiento previo                         | HR de Supervivencia global (IC95) | Número de eventos OS | HR PFS (IC95)                   | Número de eventos PFS  | Eventos adversos graves                                                                     |
|--------|----------|--------------|------|------------------------------------------|------------------------------------------------------------------------------------------------------|-------------|---------------------------|-------------------------|-----------------------------------|---------------------|-------------------------------------|--------------------------------------------|-----------------------------------|----------------------|---------------------------------|------------------------|---------------------------------------------------------------------------------------------|
|        |          |              |      |                                          |                                                                                                      |             |                           |                         | tabla, pero todos $\geq 4$ ng/mL) |                     |                                     |                                            |                                   |                      |                                 |                        | mortalidad relacionada                                                                      |
| 8      | ARCHES   | Armstrong AJ | 2019 | ECA fase III, multicéntrico, doble ciego | ADT + Enzalutamida 160 mg/d                                                                          | 574         | Media na 70 (42–92)       | Gleason $\geq 8$ : 63%  | PSA mediana 5.3 ng/mL             | 24%                 | Mixto                               | 17.7% habían recibido docetaxel previo     | HR OS 0.81 (95% CI 0.53–1.25)     | 84 muertes           | HR rPFS 0.39 (95% CI 0.30–0.50) | 91 progresiones        | EA $\geq 3$ : 24.3%; hipertensión 7%, fatiga 1.6%                                           |
| 8      | ARCHES   | Armstrong AJ | 2019 | ECA fase III, multicéntrico, doble ciego | ADT + Placebo                                                                                        | 576         | Media na 70 (44–93)       | Gleason $\geq 8$ : 64%  | PSA mediana 5.2 ng/mL             | 24%                 | Mixto                               | 17.6% habían recibido docetaxel previo     | HR OS 1.0 (comparador)            | 89 muertes           | Ref: HR 1.0 (comparador)        | 201 progresiones       | EA $\geq 3$ : 25.6%; hipertensión 5%, fatiga 1%                                             |
| 9      | ENZAMET  | Davis ID     | 2019 | ECA fase III, multicéntrico, abierto     | ADT + Enzalutamida 160 mg/d $\pm$ docetaxel temprano                                                 | 563         | Media na 69 (rango 41–92) | Gleason $\geq 8$ : ~60% | NI                                | 11%                 | Mixto                               | 45% recibieron docetaxel planificado       | HR OS 0.67 (95% CI 0.52–0.86)     | 102 muertes          | HR PFS 0.40 (95% CI 0.33–0.49)  | NI                     | EA $\geq 3$ : fatiga, hipertensión; convulsiones en 1% (7 pts); más neuropatía si docetaxel |
| 9      | ENZAMET  | Davis ID     | 2019 | ECA fase III, multicéntrico, abierto     | ADT + antiandrógeno estándar (bicalutamida 50 mg/d, nilutamida o flutamida) $\pm$ docetaxel temprano | 562         | Media na 68 (rango 42–93) | Gleason $\geq 8$ : ~60% | NI                                | 12%                 | Mixto                               | 45% recibieron docetaxel planificado       | HR OS 1.0 (comparador)            | 143 muertes          | Ref: HR 1.0 (comparador)        | NI                     | EA: menos fatiga, sin convulsiones reportadas                                               |
| 10     | LATITUDE | Fizazi K     | 2017 | ECA fase III, multicéntrico, doble ciego | ADT + Abiraterona 1000 mg/d + Prednisona 5 mg/d                                                      | 597         | Media na 68 (rango 18–89) | Gleason $\geq 8$ : 98%  | PSA mediana 45 ng/mL              | 13%                 | High                                | No (ADT naïve; excluyó tratamiento previo) | HR OS 0.62 (95% CI 0.51–0.76)     | 169 muertes (28%)    | HR rPFS 0.47 (95% CI 0.39–0.55) | 150 progresiones (25%) | EA $\geq 3$ : HTA 20%, hipopotasemia 10%, $\uparrow$ ALT/AST 6%, fatiga 4%                  |

| ID_art | Estudio           | Autor    | Año  | Tipo de estudio                                              | Tratamiento                                                | N por brazo | Edad                      | Score Gleason     | PSA medio                                            | Metástasis visceral | Análisis por subgrupo (Low vs High) | Tratamiento previo     | HR de Supervivencia global (IC95) | Número de eventos OS | HR PFS (IC95)                  | Número de eventos PFS  | Eventos adversos graves                                  |
|--------|-------------------|----------|------|--------------------------------------------------------------|------------------------------------------------------------|-------------|---------------------------|-------------------|------------------------------------------------------|---------------------|-------------------------------------|------------------------|-----------------------------------|----------------------|--------------------------------|------------------------|----------------------------------------------------------|
| 10     | LATITUDE          | Fizazi K | 2017 | ECA fase III, multicéntrico, doble ciego                     | ADT + Placebo                                              | 602         | Media na 68 (rango 18–89) | Gleason ≥8: 98%   | PSA mediana 46 ng/mL                                 | 11%                 | High                                | No                     | HR OS 1.0 (comparador)            | 246 muertes (41%)    | Ref: HR 1.0 (comparador)       | 304 progresiones (50%) | EA ≥3: HTA 10%, hipopotasemia 1%, ↑ALT/AST 1%, fatiga 2% |
| 11     | PEACE-1           | Fizazi K | 2022 | Fase III, abierto, 2x2 factorial                             | TPA + Abiraterona + Prednisona (SOC: ADT ± Docetaxel ± RT) | 583         | Media na 67               | ≥8: 57%           | NI                                                   | 12%                 | High                                | No                     | HR: 0.82 (0.69–0.98)              | 228                  | HR_0.54 (0.41–0.71)            | 259                    | ≥G3: 55 por 100 persona-años (seguridad global)          |
| 11     | PEACE-1           | Fizazi K | 2022 | Fase III, abierto, 2x2 factorial                             | TPA (SOC: ADT ± Docetaxel ± RT)                            | 589         | Media na 66               | ≥8: 57%           | NI                                                   | 12%                 | High                                | No                     | HR OS 1.0 (comparador)            | 268                  | Ref: HR 1.0 (comparador)       | 371                    | ≥G3: 40 por 100 persona-años                             |
| 12     | TITAN             | Chi KN   | 2019 | ECA fase III, multicéntrico, doble ciego                     | ADT + Apalutamida 240 mg/d                                 | 525         | Media na 69 (45–94)       | Gleason >7: 66.9% | 5.97 ng/mL (0–2682)                                  | 10.7% (56/525)      | Mixto                               | Docetaxel previo 11.0% | 0.67 (0.51–0.89)                  | 83                   | 0.48 (0.39–0.60) (rPFS)        | 134                    | ≥G3 42.2%; SAEs 19.8%; rash ≥G3 6.3%                     |
| 12     | TITAN             | Chi KN   | 2019 | ECA fase III, multicéntrico, doble ciego                     | ADT + Placebo                                              | 527         | Media na 68 (43–90)       | Gleason >7: 67.9% | 4.02 ng/mL (0–2229)                                  | 13.7% (72/527)      | Mixto                               | Docetaxel previo 10.4% | HR OS 1.0 (comparador)            | 117                  | Ref: HR 1.0 (comparador)       | 231                    | ≥G3 40.8%; SAEs 20.3%                                    |
| 13     | STAMPED E – Arm G | James ND | 2017 | ECA fase III, multicéntrico, abierto, plataforma multi-brazo | ADT + Abiraterona 1000 mg/d + Prednisona 5 mg/d            | 501 (M1)    | Media na 67 (IQR 61–72)   | Gleason ≥8: 52%   | NI (media na no reportada para M1; global ~92 ng/mL) | 17%                 | High                                | No (ADT naïve)         | HR: 0.61 (95% CI 0.49–0.75)       | 184 muertes          | 0.29 (95% CI 0.25–0.34) (rPFS) | 248 progresiones       | ≥G3: 47%; HTA ≥G3 10%, hepatotox 6%, hipopotasemia 7%    |
| 13     | STAMPED E – Arm G | James ND | 2017 | ECA fase III, multicéntrico                                  | ADT (SOC)                                                  | 502 (M1)    | Media na 66 (IQR          | Gleason ≥8: 54%   | NI                                                   | 18%                 | High                                | No                     | HR OS 1.0 (comparador)            | 262 muertes          | Ref: HR 1.0                    | 392 progresiones       | ≥G3: 33%; HTA ≥G3 4%,                                    |

| ID_art | Estudio | Autor | Año | Tipo de estudio                     | Tratamiento | N por brazo | Edad   | Score Gleason | PSA media no | Metástasis visceral | Análisis por subgrupo (Low vs High) | Tratamiento previo | HR de Supervivencia global (IC95) | Número de eventos OS | HR PFS (IC95) | Numero de eventos PFS | Eventos adversos graves          |
|--------|---------|-------|-----|-------------------------------------|-------------|-------------|--------|---------------|--------------|---------------------|-------------------------------------|--------------------|-----------------------------------|----------------------|---------------|-----------------------|----------------------------------|
|        |         |       |     | co, abierto, plataforma multi-brazo |             |             | 61–71) |               |              |                     |                                     |                    |                                   |                      | (comparador)  |                       | hepatotox <2%, hipopotasemia <1% |

## Anexo J. Script para los metaanálisis

### PREGUNTA 2 SOBREVIDA GENERAL

```
# NMA Q2 - OS (nmCRPC, con TPA) — HR
# Estudios: PROSPER / SPARTAN / ARAMIS
# =====

run_nma_q2_os_nmcrcp <- function() {
  if (!requireNamespace("netmeta", quietly = TRUE))
    install.packages("netmeta", repos = "https://cloud.r-project.org")
  library(netmeta)

  op <- options(stringsAsFactors = FALSE); on.exit(options(op), add = TRUE)
  while (!is.null(dev.list())) dev.off()

  outdir <- paste0("NMA_Q2_OS_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  raw_txt <- "
Estudio\tAutor\tAño\tTratamiento\tN_por_brazo\tHR_texto
PROSPER\tHussain\t2018\tEnzalutamida + TPA\t933\t0,73 (0.61-0.89)
PROSPER\tHussain\t2018\tPlacebo + TPA\t468\tNA
SPARTAN\tSmith\t2018\tApalutadmia + TPA\t806\t0,70 (0,47-1.04)
SPARTAN\tSmith\t2018\tPlacebo + TPA\t401\tNA
ARAMIS\tFizazi\t2019\tDarolutamida + TPA\t55\t0,71 (0,50-0,99)
ARAMIS\tFizazi\t2019\tPlacebo + TPA\t554\tNA
"

  dat0 <- read.table(text = raw_txt, header = TRUE, sep = "\t", quote = "", check.names = FALSE)
  dat0$Tratamiento <- gsub(" +", " ", trimws(dat0$Tratamiento))
  dat0$Tratamiento <- sub("^Apalutadmia", "Apalutamida", dat0$Tratamiento)

  parse_hr_ci <- function(x){
    if (is.na(x) || toupper(x) %in% c("NA", "REF", "REFERENCE")) return(c(NA, NA, NA))
    x2 <- gsub(",", ".", x)
    m <- regexec("([0-9]*\\.?[0-9]+)\\s*(\\s*([0-9]*\\.?[0-9]+)\\s*[-+])\\s*([0-9]*\\.?[0-9]+)\\s*",
x2)
    g <- regmatches(x2, m)[[1]]
    if (length(g) != 4) stop("No pude parsear: ", x)
    c(as.numeric(g[2]), as.numeric(g[3]), as.numeric(g[4]))
  }
  tmp <- t(vapply(dat0$HR_texto, parse_hr_ci, numeric(3))); colnames(tmp) <- c("HR", "LCL", "UCL")
  dat <- cbind(dat0, tmp)

  isRef <- function(x) is.na(x)
  build_pairs <- function(df){
    do.call(rbind, lapply(split(df, df$Estudio), function(d){
      base <- d[isRef(d$HR), , drop=FALSE]; if (!nrow(base)) stop("Sin ref en ", d$Estudio[1])
      base_trt <- base$Tratamiento[1]
      d1 <- d[!isRef(d$HR), , drop=FALSE]; if (!nrow(d1)) return(NULL)
      data.frame(
        studlab = paste(d1$Estudio, d1$Año),
        treat1 = d1$Tratamiento,
        treat2 = base_trt,
        TE = log(d1$HR),
        seTE = (log(d1$UCL) - log(d1$LCL))/(2*1.96),
        stringsAsFactors = FALSE
      )
    })
  })
}
```

```

}

pairs <- build_pairs(dat)
write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names=FALSE)

sink(file.path(outdir, "00_netconnection.txt"))
print(netconnection(pairs$treat1, pairs$treat2, pairs$studlab))
sink()

ref.trt <- "Placebo + TPA"
nma <- netmeta(TE=pairs$TE, seTE=pairs$seTE, treat1=pairs$treat1, treat2=pairs$treat2,
  studlab=pairs$studlab, sm="HR", common=TRUE, random=TRUE,
  reference.group=ref.trt, method.tau="REML", details=TRUE)
sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits=3); sink()

order_by_hr_vs_ref <- function(nma, ref.trt){
  nl <- netleague(nma, random=TRUE, common=FALSE)
  TEr <- nl$TE.random; SEr <- nl$seTE.random
  trts <- setdiff(nma$trts, ref.trt)
  rows <- lapply(trts, function(t){
    r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
    te <- if (!is.na(r)&&!is.na(c)) TEr[r,c] else NA_real_
    se <- if (!is.na(r)&&!is.na(c)) SEr[r,c] else NA_real_
    if (is.na(te)) { r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
      if (!is.na(r2)&&!is.na(c2)&&!is.na(TEr[r2,c2])){ te <- -TEr[r2,c2]; se <- SEr[r2,c2] } }
    data.frame(Tratamiento=t, HR=exp(te), LCL=exp(te-1.96*se), UCL=exp(te+1.96*se))
  })
  df <- do.call(rbind, rows); df <- df[order(df$HR), ]
  list(seq=c(df$Tratamiento, ref.trt), table=df)
}
ord <- order_by_hr_vs_ref(nma, ref.trt)
write.csv(ord$table, file.path(outdir, "03_forest_order_source_table.csv"), row.names=FALSE)

par(mar=c(5,5,2,2))
netgraph(nma, plastic=FALSE, multiarm=TRUE, thickness="number.of.studies",
  number.of.studies=TRUE, cex.number=0.9, points=TRUE, cex=1.2)
title(main="Estructura de la red – OS (nmCRPC, TPA)")
png(file.path(outdir, "02_network.png"), width=1400, height=1000, res=170)
par(mar=c(5,5,2,2)); netgraph(nma, plastic=FALSE, multiarm=TRUE,
  thickness="number.of.studies", number.of.studies=TRUE, cex.number=0.9, points=TRUE, cex=1.2)
title(main="Estructura de la red – OS (nmCRPC, TPA)"); dev.off()

par(mar=c(6,10,5,2))
forest(nma, ref=ref.trt, baseline=FALSE, seq=ord$seq, digits=2, smlab="HR (OS)",
  label.left="Favorece tratamiento", label.right="Favorece referencia",
  title=sprintf("Comparisons vs %s — menor HR (mejor) arriba", ref.trt))
png(file.path(outdir, "03_forest_vs_REF_order_auto.png"), width=1700, height=1500, res=170)
par(mar=c(6,10,5,2))
forest(nma, ref=ref.trt, baseline=FALSE, seq=ord$seq, digits=2, smlab="HR (OS)",
  label.left="Favorece tratamiento", label.right="Favorece referencia",
  title=sprintf("Comparisons vs %s — menor HR (mejor) arriba", ref.trt))
dev.off()

lt <- netleague(nma, random=TRUE, common=FALSE, digits=2, bracket="[" , text="HR")
sink(file.path(outdir, "04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir, "04_league_table.csv"))

side <- netsplit(nma)
sink(file.path(outdir, "05_SIDE_full.txt")); print(side, digits=3, show="all"); sink()
par(mar=c(8,22,5,4))
forest(side, digits=2, show="all", cex=0.95, title="Directo vs Indirecto (SIDE) – OS")
png(file.path(outdir, "05_SIDE_forest_large.png"), width=2400, height=2800, res=180)

```



```

par(mar=c(8,22,5,4)); forest(side, digits=2, show="all", cex=0.95,
      title="Directo vs Indirecto (SIDE) - OS"); dev.off()
sink(file.path(outdir,"05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

toRankingDF <- function(x, trts){
  if (is.null(x)) return(data.frame())
  if (is.atomic(x) && is.null(dim(x))){
    rn <- names(x); if (is.null(rn)||any(rn=="")) rn <- trts
    return(data.frame(Tratamiento=rn, Pscore=as.numeric(x),
      Rank=rank(-as.numeric(x), ties.method="average"), row.names=NULL))
  }
  df <- as.data.frame(x)
  if (is.null(rownames(df))||any(rownames(df)=="")) rownames(df) <- trts
  cn <- tolower(gsub("[^a-z]", "", colnames(df)))
  ip <- which(cn %in% c("pscore", "pscores", "p", "pscorerandom", "pscorecommon")); if(!length(ip)) ip <- 1
  ir <- which(cn %in% c("rank", "ranking", "rankrandom", "rankcommon"))
  P <- as.numeric(df[[ip[1]]]); R <- if(length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
  data.frame(Tratamiento=rownames(df), Pscore=P, Rank=R, row.names=NULL)
}
rk <- netrank(nma, small.values="good")
df_ps <- merge(
  transform(toRankingDF(rk$ranking.random, nma$trts), Pscore_random=Pscore,
    Rank_random=Rank)[,c("Tratamiento", "Pscore_random", "Rank_random")],
  transform(toRankingDF(rk$ranking.common, nma$trts), Pscore_common=Pscore,
    Rank_common=Rank)[,c("Tratamiento", "Pscore_common", "Rank_common")],
  by="Tratamiento", all=TRUE)
df_ps <- df_ps[order(-df_ps$Pscore_random), ]
write.csv(df_ps, file.path(outdir,"06_pscores.csv"), row.names=FALSE)

par(mar=c(5,5,3,2))
rankogram(nma, small.values="good", n.iter=1000); title(main="Rankogram - OS")
png(file.path(outdir,"06_rankogram.png"), width=1400, height=1100, res=170)
par(mar=c(5,5,3,2)); rankogram(nma, small.values="good", n.iter=1000); title(main="Rankogram -
OS"); dev.off()

labs_legend <- unique(paste(pairs$treat1, "vs", pairs$treat2))
par(mar=c(5,5,3,11), xpd=NA); funnel(nma, order=ord$seq, legend=FALSE); title(main="Funnel - OS")
legend("topright", inset=c(-0.35,0), legend=labs_legend, bty="n", cex=0.85)
png(file.path(outdir,"07_funnel_clean.png"), width=1700, height=1100, res=170)
par(mar=c(5,5,3,11), xpd=NA); funnel(nma, order=ord$seq, legend=FALSE); title(main="Funnel - OS")
legend("topright", inset=c(-0.35,0), legend=labs_legend, bty="n", cex=0.85); dev.off()

ok_heat <- TRUE
tryCatch({
  par(mar=c(5,5,3,2)); netheat(nma); title(main="Net heat - OS")
  png(file.path(outdir,"08_heat.png"), width=1400, height=1100, res=170)
  par(mar=c(5,5,3,2)); netheat(nma); title(main="Net heat - OS"); dev.off()
}, warning=function(w) ok_heat <- FALSE, error=function(e) ok_heat <- FALSE)
if (!ok_heat)
  writeLines(c("Net heat plot no disponible:",
    "- La red no contiene bucles (estructura en estrella)."),
    file.path(outdir,"08_heat_NOT_AVAILABLE.txt"))

interp <- transform(ord$table,
  Interpretacion = ifelse(UCL<1,"Beneficio OS vs ref",
    ifelse(LCL>1,"Peor OS vs ref", "No concluyente")))
write.csv(interp, file.path(outdir,"09_interpretacion_clinica.csv"), row.names=FALSE)

cat("\nListo. Carpeta:", outdir, "\n")
print(list.files(outdir))
}
# Ejecuta: # run_nma_q2_os_nmcrpc()

```

## PREGUNTA 2\_PFS-MFS Y EA

```
# =====
# Utilidades comunes para los 3 NMA
# =====
if (!requireNamespace("netmeta", quietly = TRUE))
  install.packages("netmeta", repos = "https://cloud.r-project.org")
library(netmeta)

options(stringsAsFactors = FALSE)

# Parser genérico "0,29 (0,24-0,35)" -> c(HR, LCL, UCL)
.parse_hr_ci <- function(x) {
  if (is.na(x) || toupper(trimws(x)) %in% c("NA", "REF", "REFERENCE")) return(c(NA, NA, NA))
  x2 <- gsub(",", ".", trimws(x))
  m <- regexec("([0-9]*\\.?[0-9]+)\\s*\\(\\s*([0-9]*\\.?[0-9]+)\\s*[-]\\s*([0-9]*\\.?[0-9]+)\\s*\\)", x2)
  g <- regmatches(x2, m)[[1]]
  if (length(g) != 4) stop("No pude parsear: ", x)
  as.numeric(g[2:4])
}

# Construye pares (tratamiento vs brazo referencia NA/Ref en cada estudio)
.build_pairs_HR <- function(df, study_col, trt_col, hr_col, lcl_col, ucl_col, year_col) {
  do.call(rbind, lapply(split(df, df[[study_col]]), function(d) {
    base <- d[is.na(d[[hr_col]]), , drop = FALSE]
    if (nrow(base) == 0) stop("No hallé brazo de referencia (NA) en estudio: ", d[[study_col]][1])
    base_trt <- base[[trt_col]][1]
    d1 <- d[!is.na(d[[hr_col]]), , drop = FALSE]
    if (!nrow(d1)) return(NULL)
    data.frame(
      studlab = paste(d1[[study_col]], d1[[year_col]]),
      treat1 = d1[[trt_col]],
      treat2 = base_trt,
      TE = log(d1[[hr_col]]),
      seTE = (log(d1[[ucl_col]]) - log(d1[[lcl_col]])) / (2*1.96),
      stringsAsFactors = FALSE
    )
  }))
}

# Orden por efecto puntual (random) Tratamiento→Referencia
.order_by_vs_ref <- function(nma, ref.trt, label = c("HR", "RR")) {
  label <- match.arg(label)
  nl <- netleague(nma, random = TRUE, common = FALSE)
  TEr <- nl$TE.random; SEr <- nl$seTE.random
  trts <- setdiff(nma$trts, ref.trt)
  rows <- lapply(trts, function(t){
    r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
    te <- if (!is.na(r) && !is.na(c)) TEr[r,c] else NA_real_
    se <- if (!is.na(r) && !is.na(c)) SEr[r,c] else NA_real_
    if (is.na(te)) { r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
      if (!is.na(r2) && !is.na(c2) && !is.na(TEr[r2,c2])) { te <- -TEr[r2,c2]; se <- SEr[r2,c2] } }
    val <- exp(te); lcl <- exp(te-1.96*se); ucl <- exp(te+1.96*se)
    setNames(data.frame(Tratamiento=t, Valor=val, LCL=lcl, UCL=ucl), c("Tratamiento", label, "LCL", "UCL"))
  })
  df <- do.call(rbind, rows)
  df <- df[order(df[[label]], decreasing = FALSE), ]
  list(seq = c(df$Tratamiento, ref.trt), table = df)
}
```

```

}

# Helper de guardado: muestra y guarda
.show_and_save <- function(file, width, height, res, plot_fun) {
  plot_fun()
  png(file, width = width, height = height, res = res, pointsize = 11)
  plot_fun()
  dev.off()
}

# =====
# 1) PSA-PFS (HR) — PROSPER / SPARTAN / ARAMIS / STRIVE
# =====
run_nma_q2_psa_pfs <- function() {
  while (!is.null(dev.list())) dev.off()
  outdir <- paste0("NMA_Q2_PSA_PFS_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  raw_txt <- "
Estudio\tAutor\tAño\tTipo_de_estudio\tTratamiento\tN_por_brazo\tHR_text
PROSPER\tHussain\t2018\tEnsayo clínico\tEnzalutamida + TPA\t933\t0,07 (0,05-0,08)
PROSPER\tHussain\t2018\tEnsayo clínico\tPlacebo + TPA\t468\tNA
SPARTAN\tSmith\t2018\tEnsayo clínico\tApalutadmia + TPA\t806\t0,06 (0,05-0,08)
SPARTAN\tSmith\t2018\tEnsayo clínico\tPlacebo + TPA\t401\tNA
ARAMIS\tFizazi\t2019\tEnsayo clínico\tDarolutamida + TPA\t55\t0,13 (0,11-0,16)
ARAMIS\tFizazi\t2019\tEnsayo clínico\tPlacebo + TPA\t554\tNA
STRIVE\tPenson\t2016\tEnsayo clínico\tEnzalutamida + TPA\t140\t0,18 (0,10-0,34)
STRIVE\tPenson\t2016\tEnsayo clínico\tBicalutamida + TPA\t138\tNA
"

  d0 <- read.table(text = raw_txt, header = TRUE, sep = "\t", quote = "", check.names = FALSE)
  names(d0)[names(d0)=="Tipo_de_estudio"] <- "Tipo de estudio"
  d0$Tratamiento <- gsub(" +", " ", trimws(d0$Tratamiento))
  d0$Tratamiento <- sub("^Apalutadmia", "Apalutamida", d0$Tratamiento)

  tmp <- t(vapply(d0$HR_text, .parse_hr_ci, numeric(3)))
  colnames(tmp) <- c("HR", "LCL", "UCL")
  dat <- cbind(d0, tmp)

  write.csv(dat, file.path(outdir, "00_dataset_parsed.csv"), row.names = FALSE)

  pairs <- .build_pairs_HR(dat, "Estudio", "Tratamiento", "HR", "LCL", "UCL", "Año")
  write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names = FALSE)

  sink(file.path(outdir, "00_netconnection.txt"))
  print(netconnection(treat1 = pairs$treat1, treat2 = pairs$treat2, studlab = pairs$studlab))
  sink()

  ref.trt <- "Placebo + TPA"
  nma <- netmeta(TE = pairs$TE, seTE = pairs$seTE,
    treat1 = pairs$treat1, treat2 = pairs$treat2,
    studlab = pairs$studlab, sm = "HR",
    common = TRUE, random = TRUE,
    reference.group = ref.trt, method.tau = "REML",
    details = TRUE)
  sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits = 3); sink()

  # Network
  net_fun <- function(){
    par(mar = c(5,5,2,2))
    netgraph(nma, plastic = FALSE, multiarm = TRUE,
      thickness = "number.of.studies", number.of.studies = TRUE,
      cex.number = 0.9, points = TRUE, cex = 1.2)
  }

```

```

    title(main = "Red - PSA-PFS (HR)")
  }
  .show_and_save(file.path(outdir,"02_network.png"), 1400, 1000, 170, net_fun)

# Forest
ord <- .order_by_vs_ref(nma, ref.trt, label = "HR")
write.csv(ord$table, file.path(outdir,"03_forest_order_source_table.csv"), row.names = FALSE)

forest_fun <- function(){
  par(mar = c(6,10,5,2))
  forest(nma, ref = ref.trt, baseline = FALSE, seq = ord$seq,
    digits = 2, smlab = "HR (PSA-PFS)",
    label.left = "Mejor (↓HR)", label.right = "Peor (↑HR)")
  mtext(sprintf("Comparisons vs %s — menor HR (mejor) arriba", ref.trt), side = 3, line = 0.2)
}
.show_and_save(file.path(outdir,"03_forest_vs_REF_order_auto.png"), 1700, 1500, 170, forest_fun)

# League table
lt <- netleague(nma, random = TRUE, common = FALSE, digits = 2, bracket = "[", text = "HR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

# SIDE + Q
side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits = 3, show = "all"); sink()
side_fun <- function(){
  par(mar = c(8,22,5,4))
  forest(side, digits = 2, show = "all", cex = 0.95, title = "SIDE — PSA-PFS (HR)")
}
.show_and_save(file.path(outdir,"05_SIDE_forest_large.png"), 2400, 2800, 180, side_fun)
sink(file.path(outdir,"05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

# Rankings / P-scores
rk <- netrank(nma, small.values = "good")
toDF <- function(x, trts){
  if (is.null(x)) return(data.frame())
  if (is.atomic(x) && is.null(dim(x))) {
    rn <- names(x); if (is.null(rn) || any(rn=="")) rn <- trts
    return(data.frame(Tratamiento = rn, Pscore = as.numeric(x),
      Rank = rank(-as.numeric(x), ties.method = "average")))
  }
  df <- as.data.frame(x); if (is.null(rownames(df)) || any(rownames(df)=="")) rownames(df) <- trts
  cn <- tolower(gsub("[^a-z]", "", colnames(df)))
  ip <- which(cn %in% c("pscore", "pscores", "p", "pscorerandom", "pscorecommon")); if (!length(ip)) ip <- 1
  ir <- which(cn %in% c("rank", "ranking", "rankrandom", "rankcommon"))
  P <- as.numeric(df[[ip[1]]]); R <- if (length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
  data.frame(Tratamiento=rownames(df), Pscore=P, Rank=R)
}
dfr <- toDF(rk$ranking.random, nma$trts)
dfc <- toDF(rk$ranking.common, nma$trts)
out <- merge(transform(dfr, Pscore_random=Pscore,
  Rank_random=Rank)[,c("Tratamiento", "Pscore_random", "Rank_random")],
  transform(dfc, Pscore_common=Pscore,
  Rank_common=Rank)[,c("Tratamiento", "Pscore_common", "Rank_common")],
  by="Tratamiento", all=TRUE)
write.csv(out[order(-out$Pscore_random),], file.path(outdir,"06_pscores.csv"), row.names = FALSE)

# Rankogram
rank_fun <- function(){ par(mar=c(5,5,3,2)); rankogram(nma, small.values="good", n.iter=1000);
title(main="Rankogram — PSA-PFS") }
.show_and_save(file.path(outdir,"06_rankogram.png"), 1400, 1100, 170, rank_fun)

```

```
# Funnel (leyenda fuera)
labs_legend <- unique(paste(pairs$treat1, "vs", pairs$treat2))
funnel_fun <- function(){
  par(mar=c(5,5,3,11), xpd=NA)
  funnel(nma, order = ord$seq, legend = FALSE); title(main="Funnel — PSA-PFS")
  legend("topright", inset=c(-0.35,0), legend=labs_legend, bty="n", cex=0.85)
}
.show_and_save(file.path(outdir,"07_funnel_clean.png"), 1700, 1100, 170, funnel_fun)

# Net heat
ok <- TRUE
tryCatch({
  heat_fun <- function(){ par(mar=c(5,5,3,2)); netheat(nma); title(main="Net heat — PSA-PFS") }
  .show_and_save(file.path(outdir,"08_heat.png"), 1400, 1100, 170, heat_fun)
}, warning=function(w) ok<-FALSE, error=function(e) ok<-FALSE)
if (!ok) writeLines(c("Net heat no disponible", "- No hay bucles cerrados"),
file.path(outdir,"08_heat_NOT_AVAILABLE.txt"))

# Interpretación clínica
inter <- transform(ord$table, Interpretacion = ifelse(UCL<1,"Mejor vs ref", ifelse(LCL>1,"Peor vs ref","No
concluyente")))
write.csv(inter, file.path(outdir,"09_interpretacion_clinica.csv"), row.names = FALSE)

cat("Listo PSA-PFS. Carpeta:", outdir, "\n")
}

# =====
# 2) MFS (HR) — PROSPER / SPARTAN / ARAMIS
# =====
run_nma_q2_mfs <- function() {
  while (!is.null(dev.list())) dev.off()
  outdir <- paste0("NMA_Q2_MFS_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  raw_txt <- "
Estudio\tAutor\tAño\tTipo_de_estudio\tTratamiento\tN_por_brazo\tHR_text
PROSPER\tHussain\t2018\tEnsayo clínico\tEnzalutamida + TPA\t933\t0,29 (0,24-0,35)
PROSPER\tHussain\t2018\tEnsayo clínico\tPlacebo + TPA\t468\tNA
SPARTAN\tSmith\t2018\tEnsayo clínico\tApalutadmia + TPA\t806\t0,28 (0,23-0,35)
SPARTAN\tSmith\t2018\tEnsayo clínico\tPlacebo + TPA\t401\tNA
ARAMIS\tFizazi\t2019\tEnsayo clínico\tDarolutamida + TPA\t55\t0,41 (0,34-0,50)
ARAMIS\tFizazi\t2019\tEnsayo clínico\tPlacebo + TPA\t554\tNA
"

  d0 <- read.table(text = raw_txt, header = TRUE, sep = "\t", quote = "", check.names = FALSE)
  names(d0)[names(d0)=="Tipo_de_estudio"] <- "Tipo de estudio"
  d0$Tratamiento <- gsub(" +", " ", trimws(d0$Tratamiento))
  d0$Tratamiento <- sub("^Apalutadmia", "Apalutamida", d0$Tratamiento)

  tmp <- t(vapply(d0$HR_text, .parse_hr_ci, numeric(3)))
  colnames(tmp) <- c("HR", "LCL", "UCL")
  dat <- cbind(d0, tmp)
  write.csv(dat, file.path(outdir,"00_dataset_parsed.csv"), row.names = FALSE)

  pairs <- .build_pairs_HR(dat, "Estudio", "Tratamiento", "HR", "LCL", "UCL", "Año")
  write.csv(pairs, file.path(outdir,"00_pairwise_dataset.csv"), row.names = FALSE)

  sink(file.path(outdir,"00_netconnection.txt"))
  print(netconnection(treat1=pairs$treat1, treat2=pairs$treat2, studlab=pairs$studlab))
  sink()

  ref.trt <- "Placebo + TPA"
  nma <- netmeta(TE=pairs$TE, seTE=pairs$seTE, treat1=pairs$treat1, treat2=pairs$treat2,
```

```

studlab=pairs$studlab, sm="HR", common=TRUE, random=TRUE,
reference.group=ref.trt, method.tau="REML", details=TRUE)
sink(file.path(outdir,"01_NMA_summary.txt")); print(nma, digits=3); sink()

net_fun <- function(){ par(mar=c(5,5,2,2)); netgraph(nma, plastic=FALSE, multiarm=TRUE,
thickness="number.of.studies", number.of.studies=TRUE,
cex.number=0.9, points=TRUE, cex=1.2); title(main="Red – MFS (HR)") }
.show_and_save(file.path(outdir,"02_network.png"), 1400, 1000, 170, net_fun)

ord <- .order_by_vs_ref(nma, ref.trt, label="HR")
write.csv(ord$table, file.path(outdir,"03_forest_order_source_table.csv"), row.names=FALSE)

forest_fun <- function(){ par(mar=c(6,10,5,2)); forest(nma, ref=ref.trt, baseline=FALSE, seq=ord$seq,
digits=2, smlab="HR (MFS)", label.left="Mejor (↓HR)", label.right="Peor (↑HR)");
mtext(sprintf("Comparisons vs %s — menor HR (mejor arriba", ref.trt), side=3,
line=0.2) }
.show_and_save(file.path(outdir,"03_forest_vs_REF_order_auto.png"), 1700, 1500, 170, forest_fun)

lt <- netleague(nma, random=TRUE, common=FALSE, digits=2, bracket="[" , text="HR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits=3, show="all"); sink()
side_fun <- function(){ par(mar=c(8,22,5,4)); forest(side, digits=2, show="all", cex=0.95, title="SIDE —
MFS (HR)") }
.show_and_save(file.path(outdir,"05_SIDE_forest_large.png"), 2400, 2800, 180, side_fun)
sink(file.path(outdir,"05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

rk <- netranks(nma, small.values="good")
toDF <- function(x,trts){ if(is.null(x)) return(data.frame());
if(is.atomic(x) && is.null(dim(x))){ rn<-names(x); if(is.null(rn)||any(rn=="")) rn<-trts;
return(data.frame(Tratamiento=rn, Pscore=as.numeric(x), Rank=rank(-as.numeric(x),
ties.method="average")))} }
df<-as.data.frame(x); if(is.null(row.names(df))||any(row.names(df)=="")) row.names(df)<-trts
cn<-tolower(gsub("[^a-z]", "",colnames(df))); ip<-which(cn %in%
c("pscore","pscores","p","pscorerandom","pscorecommon")); if(!length(ip)) ip<-1
ir<-which(cn %in% c("rank","ranking","rankrandom","rankcommon")); P<-as.numeric(df[[ip[1]]]); R<-
if(length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
data.frame(Tratamiento=row.names(df), Pscore=P, Rank=R)
}
dfr<-toDF(rk$ranking.random, nma$trts); dfc<-toDF(rk$ranking.common, nma$trts)
out<-merge(transform(dfr, Pscore_random=Pscore,
Rank_random=Rank)[,c("Tratamiento","Pscore_random","Rank_random")],
transform(dfc, Pscore_common=Pscore,
Rank_common=Rank)[,c("Tratamiento","Pscore_common","Rank_common")],
by="Tratamiento", all=TRUE)
write.csv(out[order(-out$Pscore_random),], file.path(outdir,"06_pscores.csv"), row.names=FALSE)

rank_fun <- function(){ par(mar=c(5,5,3,2)); rankogram(nma, small.values="good", n.iter=1000);
title(main="Rankogram — MFS") }
.show_and_save(file.path(outdir,"06_rankogram.png"), 1400, 1100, 170, rank_fun)

labs <- unique(paste(pairs$treat1, "vs", pairs$treat2))
funnel_fun <- function(){ par(mar=c(5,5,3,11), xpd=NA); funnel(nma, order=ord$seq, legend=FALSE);
title(main="Funnel — MFS"); legend("topright", inset=c(-0.35,0), legend=labs, bty="n", cex=0.85) }
.show_and_save(file.path(outdir,"07_funnel_clean.png"), 1700, 1100, 170, funnel_fun)

ok <- TRUE
tryCatch({ heat_fun <- function(){ par(mar=c(5,5,3,2)); netheat(nma); title(main="Net heat — MFS") }
.show_and_save(file.path(outdir,"08_heat.png"), 1400, 1100, 170, heat_fun)},
warning=function(w) ok<-FALSE, error=function(e) ok<-FALSE)

```

```

if (!ok) writeLines(c("Net heat no disponible", "- No hay bucles cerrados"),
file.path(outdir, "08_heat_NOT_AVAILABLE.txt"))

inter <- transform(ord$table, Interpretacion = ifelse(UCL<1, "Mejor vs ref", ifelse(LCL>1, "Peor vs ref", "No
concluyente"))
write.csv(inter, file.path(outdir, "09_interpretacion_clinica.csv"), row.names=FALSE)

cat("Listo MFS. Carpeta:", outdir, "\n")
}

# =====
# 3) SAE (RR) — PROSPER / SPARTAN / ARAMIS / STRIVE
# =====
run_nma_q2_rr_sae <- function() {
  while (!is.null(dev.list())) dev.off()
  outdir <- paste0("NMA_Q2_RR_SAE_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  raw_txt <- "
Estudio\tAutor\tAño\tTipo_de_estudio\tTratamiento\tN_por_brazo\tSAE_total
PROSPER\tHussain\t2018\tEnsayo clínico\tEnzalutamida + TPA\t933\t226
PROSPER\tHussain\t2018\tEnsayo clínico\tPlacebo + TPA\t468\t85
SPARTAN\tSmith\t2018\tEnsayo clínico\tApalutamida + TPA\t806\t199
SPARTAN\tSmith\t2018\tEnsayo clínico\tPlacebo + TPA\t401\t92
ARAMIS\tFizazi\t2019\tEnsayo clínico\tDarolutamida + TPA\t55\t237
ARAMIS\tFizazi\t2019\tEnsayo clínico\tPlacebo + TPA\t554\t111
STRIVE\tPenson\t2016\tEnsayo clínico\tEnzalutamida + TPA\t140\t58
STRIVE\tPenson\t2016\tEnsayo clínico\tBicalutamida + TPA\t138\t56
"

  d0 <- read.table(text = raw_txt, header = TRUE, sep = "\t", quote = "", check.names = FALSE)
  names(d0)[names(d0)=="Tipo_de_estudio"] <- "Tipo de estudio"
  d0$Tratamiento <- gsub(" +", " ", trimws(d0$Tratamiento))

  # QC: eventos <= N
  bad <- which(d0$SAE_total > d0$N_por_brazo)
  if (length(bad)) {
    writeLines(c("ATENCIÓN: SAE_total > N_por_brazo — filas excluidas:",
      capture.output(print(d0[bad, ])),
      file.path(outdir, "00_DATA_ISSUES.txt"))
    d0 <- d0[-bad, , drop = FALSE]
  }
  write.csv(d0, file.path(outdir, "00_dataset_clean.csv"), row.names = FALSE)

  # Pares RR con continuidad 0.5
  pw <- pairwise(treat = Tratamiento, event = SAE_total, n = N_por_brazo,
    studlab = Estudio, data = d0, sm = "RR",
    add = 0.5, allstudies = TRUE)
  pairs <- with(pw, data.frame(studlab, treat1, treat2, TE, seTE))
  write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names = FALSE)

  sink(file.path(outdir, "00_netconnection.txt"))
  print(netconnection(treat1=pairs$treat1, treat2=pairs$treat2, studlab=pairs$studlab))
  sink()

  ref.trt <- "Placebo + TPA"
  nma <- netmeta(TE=pairs$TE, seTE=pairs$seTE,
    treat1=pairs$treat1, treat2=pairs$treat2,
    studlab=pairs$studlab, sm="RR",
    common=TRUE, random=TRUE,
    reference.group=ref.trt, method.tau="REML",
    details=TRUE)
  sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits=3); sink()

```

```

net_fun <- function(){ par(mar=c(5,5,2,2)); netgraph(nma, plastic=FALSE, multiarm=TRUE,
  thickness="number.of.studies", number.of.studies=TRUE,
  cex.number=0.9, points=TRUE, cex=1.2); title(main="Red - SAE (RR)") }
.show_and_save(file.path(outdir,"02_network.png"), 1400, 1000, 170, net_fun)

ord <- .order_by_vs_ref(nma, ref.trt, label="RR")
write.csv(ord$table, file.path(outdir,"03_forest_order_source_table.csv"), row.names=FALSE)

forest_fun <- function(){ par(mar=c(6,10,5,2)); forest(nma, ref=ref.trt, baseline=FALSE, seq=ord$seq,
  digits=2, smlab="RR (SAE)",
  label.left="Menos SAE (mejor)", label.right="Más SAE (peor)");
  mtext(sprintf("Comparisons vs %s — menor RR (mejor) arriba", ref.trt), side=3,
line=0.2) }
.show_and_save(file.path(outdir,"03_forest_vs_REF_order_auto.png"), 1700, 1500, 170, forest_fun)

lt <- netleague(nma, random=TRUE, common=FALSE, digits=2, bracket="[" , text="RR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits=3, show="all"); sink()
side_fun <- function(){ par(mar=c(8,22,5,4)); forest(side, digits=2, show="all", cex=0.95, title="SIDE —
SAE (RR)") }
.show_and_save(file.path(outdir,"05_SIDE_forest_large.png"), 2400, 2800, 180, side_fun)
sink(file.path(outdir,"05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

rk <- netrank(nma, small.values="good")
toDF <- function(x,trts){ if(is.null(x)) return(data.frame());
  if(is.atomic(x) && is.null(dim(x))){ rn<-names(x); if(is.null(rn)||any(rn=="")) rn<-trts;
  return(data.frame(Tratamiento=rn, Pscore=as.numeric(x), Rank=rank(-as.numeric(x),
ties.method="average")))} }
df<-as.data.frame(x); if(is.null(rownames(df))||any(rownames(df)=="")) rownames(df)<-trts
cn<-tolower(gsub("[^a-z]", "",colnames(df))); ip<-which(cn %in%
c("pscore","pscores","p","pscorerandom","pscorecommon")); if(!length(ip)) ip<-1
ir<-which(cn %in% c("rank","ranking","rankrandom","rankcommon")); P<-as.numeric(df[[ip[1]]]); R<-
if(length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
data.frame(Tratamiento=rownames(df), Pscore=P, Rank=R)
}
dfr<-toDF(rk$ranking.random, nma$trts); dfc<-toDF(rk$ranking.common, nma$trts)
out<-merge(transform(dfr, Pscore_random=Pscore,
Rank_random=Rank)[,c("Tratamiento","Pscore_random","Rank_random")],
transform(dfc, Pscore_common=Pscore,
Rank_common=Rank)[,c("Tratamiento","Pscore_common","Rank_common")],
by="Tratamiento", all=TRUE)
write.csv(out[order(-out$Pscore_random),], file.path(outdir,"06_pscores.csv"), row.names=FALSE)

rank_fun <- function(){ par(mar=c(5,5,3,2)); rankogram(nma, small.values="good", n.iter=1000);
title(main="Rankogram — SAE (RR)") }
.show_and_save(file.path(outdir,"06_rankogram.png"), 1400, 1100, 170, rank_fun)

labs <- unique(paste(pairs$treat1, "vs", pairs$treat2))
funnel_fun <- function(){ par(mar=c(5,5,3,11), xpd=NA); funnel(nma, order=ord$seq, legend=FALSE);
title(main="Funnel — SAE (RR)"); legend("topright", inset=c(-0.35,0), legend=labs, bty="n", cex=0.85) }
.show_and_save(file.path(outdir,"07_funnel_clean.png"), 1700, 1100, 170, funnel_fun)

ok <- TRUE
tryCatch({ heat_fun <- function(){ par(mar=c(5,5,3,2)); netheat(nma); title(main="Net heat — SAE
(RR)") }
.show_and_save(file.path(outdir,"08_heat.png"), 1400, 1100, 170, heat_fun)},
warning=function(w) ok<-FALSE, error=function(e) ok<-FALSE)

```



```

if (!ok) writeLines(c("Net heat no disponible", "- No hay bucles cerrados"),
file.path(outdir, "08_heat_NOT_AVAILABLE.txt"))

inter <- transform(ord$table, Interpretacion = ifelse(UCL<1, "Menos SAE vs ref (mejor)",
                                                    ifelse(LCL>1, "Más SAE vs ref (peor)", "No concluyente")))
write.csv(inter, file.path(outdir, "09_interpretacion_clinica.csv"), row.names=FALSE)

cat("Listo SAE (RR). Carpeta:", outdir, "\n")
}

# =====
# Cómo ejecutar:
# =====
# run_nma_q2_psa_pfs()
# run_nma_q2_mfs()
# run_nma_q2_rr_sae()

```

### PREGUNTA 3 SOBREVIDA GENERAL

```

## =====
## NMA – OS (HR_OS) | consola + archivos | orden automático
## =====

## 0) Paquete
if (!requireNamespace("netmeta", quietly = TRUE))
  install.packages("netmeta", repos = "https://cloud.r-project.org")
library(netmeta)

## 0.1) Limpieza gráfica por si el dispositivo quedó "raro"
graphics.off(); layout(1); par(mfrow=c(1,1), mar=c(5.1,4.1,4.1,2.1))

## 1) Carpeta de salida
outdir <- "NMA_output_OS_full"
dir.create(outdir, showWarnings = FALSE)

## 1.1) Helper: dibuja en consola y guarda PNG
plot_and_save <- function(file, expr,
                          width=1400, height=1000, res=170, pointsize=12,
                          mar=c(5.1,4.1,4.1,2.1)) {
  op <- par(no.readonly = TRUE); on.exit(par(op), add = TRUE)
  layout(1); par(mfrow=c(1,1), mar=mar)
  eval.parent(substitute(expr))
  png(file, width=width, height=height, res=res, pointsize=pointsize)
  layout(1); par(mfrow=c(1,1), mar=mar)
  eval.parent(substitute(expr))
  dev.off()
}

## 2) Datos (NO necesitas archivo)
raw_txt <- "
ID_art\tEstudio\tAutor\tAño\tTratamiento\tN_por_brazo\tHR_OS\tIC_Inf\tIC_Sup
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT + Bicalutamida\t404\t0.97\t0.7\t1.35
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT + Flutamida\t409\tRef\tRef\tRef
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT + Bicalutamida\t404\t0.88\t0.69\t1.11
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT + Flutamida\t409\tRef\tRef\tRef
3\tKYUCOG-1401\tYokomizo A\t2024\tADT\t100\t1.17\t0.69\t1.96
3\tKYUCOG-1401\tYokomizo A\t2024\tADT + Bicalutamida\t98\tRef\tRef\tRef
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT + Bicalutamida\t404\t0.87\t0.72\t1.05
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT + Flutamida\t409\tRef\tRef\tRef

```

```

7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Enzalutamida\t36\t0.31\t0.13\t0.74
7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Bicalutamida\t35\tRef\tRef\tRef
8\tARCHES\tArmstrong AJ\t2019\tADT + Enzalutamida\t574\t0.81\t0.53\t1.25
8\tARCHES\tArmstrong AJ\t2019\tADT\t576\tRef\tRef\tRef
9\tENZAMET\tDavis ID\t2019\tADT + Enzalutamida\t563\t0.67\t0.52\t0.86
9\tENZAMET\tDavis ID\t2019\tADT + Antiandr geno Noesteroideo\t562\tRef\tRef\tRef
10\tLATITUDE\tFizazi K\t2017\tADT + Abiraterona\t597\t0.62\t0.51\t0.76
10\tLATITUDE\tFizazi K\t2017\tADT\t602\tRef\tRef\tRef
11\tPEACE-1\tFizazi K\t2022\tADT + Abiraterona\t583\t0.82\t0.69\t0.98
11\tPEACE-1\tFizazi K\t2022\tADT\t589\tRef\tRef\tRef
12\tTITAN\tChi KN\t2019\tADT + Apalutamida\t525\t0.67\t0.51\t0.89
12\tTITAN\tChi KN\t2019\tADT\t527\tRef\tRef\tRef
13\tSTAMPEDE - Arm G\tJames ND\t2017\tADT + Abiraterona\t501\t0.61\t0.49\t0.75
13\tSTAMPEDE - Arm G\tJames ND\t2017\tADT\t502\tRef\tRef\tRef
"

```

```

dat0 <- read.table(text=raw_txt, header=TRUE, sep="\t", quote="",
  check.names=FALSE, stringsAsFactors=FALSE)

```

```

## 3) Pares vs 'Ref' por estudio

```

```

isRef <- function(x) is.na(suppressWarnings(as.numeric(x))) |
  toupper(trimws(x)) %in% c("REF", "REFERENCE")

```

```

pairs <- do.call(rbind, lapply(split(dat0, dat0$ID_art), function(d) {
  base <- d[isRef(d$HR_OS), , drop=FALSE]
  if (nrow(base) == 0) stop("Sin 'Ref' en ID_art=", d$ID_art[1])
  base_trt <- base$Tratamiento[1]
  d <- d[!isRef(d$HR_OS), , drop=FALSE]
  if (!nrow(d)) return(NULL)
  data.frame(
    studlab = paste(d$Estudio, d$A o),
    treat1 = d$Tratamiento,
    treat2 = base_trt,
    TE = log(as.numeric(d$HR_OS)),
    seTE = (log(as.numeric(d$IC_Sup)) - log(as.numeric(d$IC_Inf))) / (2*1.96),
    stringsAsFactors = FALSE
  )
}))
write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names=FALSE)

```

```

## 4) NMA (HR), ref = ADT

```

```

ref.trt <- "ADT"
nma <- netmeta(TE=TE, seTE=seTE,
  treat1=treat1, treat2=treat2,
  studlab=studlab, data=pairs,
  sm="HR", common=TRUE, random=TRUE,
  reference.group=ref.trt, method.tau="REML",
  details=TRUE)
sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits=3); sink()

```

```

## 5) Red

```

```

plot_and_save(file.path(outdir, "02_network.png"),
  netgraph(nma, plastic=FALSE, multiarm=TRUE,
    thickness="number.of.studies", number.of.studies=TRUE,
    cex.number=0.9, points=TRUE, cex=1.2)
)

```

```

## 6) Forest ORDENADO por HR (random) vs ADT

```

```

compute_hr_vs_ref <- function(nma, ref.trt) {
  te <- nma$TE.random; se <- nma$seTE.random
  trts <- setdiff(nma$trts, ref.trt)

  get_from_matrix <- function(te_mat, se_mat, ref, t) {

```

```

r <- match(ref, rownames(te_mat)); c <- match(t, colnames(te_mat))
te <- if (!is.na(r) && !is.na(c)) te_mat[r,c] else NA_real_
se <- if (!is.na(r) && !is.na(c)) se_mat[r,c] else NA_real_
if (is.na(te) || is.na(se)) {
  r2 <- match(t, rownames(te_mat)); c2 <- match(ref, colnames(te_mat))
  if (!is.na(r2) && !is.na(c2) && !is.na(te_mat[r2,c2])) {
    te <- -te_mat[r2,c2]; se <- se_mat[r2,c2]
  }
}
list(te=te, se=se)
}

if (is.numeric(te) && is.null(dim(te)) && length(te) > 0 && length(te) <= length(trts)+2) {
  nm <- names(te); if (is.null(nm) || length(nm)==0) nm <- trts
  se_vec <- if (!is.null(names(se)) && length(names(se))) se[nm] else se[seq_along(nm)]
  te_num <- as.numeric(te[seq_along(nm)]); se_num <- as.numeric(se_vec)
  return(data.frame(
    Tratamiento = nm,
    HR = exp(te_num),
    LCL = exp(te_num - 1.96*se_num),
    UCL = exp(te_num + 1.96*se_num),
    row.names=NULL, check.names=FALSE
  ))
}
if (is.matrix(te) && is.matrix(se)) {
  rows <- lapply(trts, function(t) {
    z <- get_from_matrix(te, se, ref.trt, t)
    data.frame(Tratamiento=t,
      HR=exp(z$te),
      LCL=exp(z$te - 1.96*z$se),
      UCL=exp(z$te + 1.96*z$se))
  })
  return(do.call(rbind, rows))
}
nl <- netleague(nma, random=TRUE, common=FALSE)
TEr <- nl$TE.random; SEr <- nl$seTE.random
rows <- lapply(trts, function(t) {
  r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
  te1 <- if (!is.na(r)&&!is.na(c)) TEr[r,c] else NA_real_
  se1 <- if (!is.na(r)&&!is.na(c)) SEr[r,c] else NA_real_
  if (is.na(te1) || is.na(se1)) {
    r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
    if (!is.na(r2)&&!is.na(c2) && !is.na(TEr[r2,c2])) { te1 <- -TEr[r2,c2]; se1 <- SEr[r2,c2] }
  }
  data.frame(Tratamiento=t,
    HR=exp(te1),
    LCL=exp(te1 - 1.96*se1),
    UCL=exp(te1 + 1.96*se1))
})
do.call(rbind, rows)
}
hr_tab <- compute_hr_vs_ref(nma, ref.trt)
hr_tab <- hr_tab[order(hr_tab$HR, decreasing=FALSE), ]
write.csv(hr_tab, file.path(outdir,"03a_HR_vs_ADT_random_table.csv"), row.names=FALSE)

orden_auto <- c(hr_tab$Tratamiento, ref.trt)
plot_and_save(file.path(outdir,"03b_forest_vs_ADT_order_auto.png"),
  forest(nma, ref=ref.trt, seq=orden_auto,
    baseline=FALSE, drop=TRUE, digits=2, smlab="HR (OS)",
    title="Comparison: other treatments vs 'ADT' (Random Effects)",
    width=1800, height=1600, res=180
  )
)

```

```
## 7) League table
lt <- netleague(nma, random=TRUE, common=FALSE, digits=2, bracket="[" , text="HR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

## 8) SIDE (grande)
side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits=3, show="all"); sink()
sdf <- tryCatch(as.data.frame(side), error=function(e) NULL)
ncomp <- if (!is.null(sdf)) nrow(sdf) else 30L
height_px <- max(3000, 700 + 90*ncomp)
plot_and_save(file.path(outdir,"05_SIDE_forest_large.png"),
  { op <- par(mar=c(10,22,6,6)); on.exit(par(op), add=TRUE)
    forest(side, digits=2, show="all", cex=0.9,
      title="Comparación directa vs indirecta (SIDE) - HR (OS)" },
  width=2500, height=height_px, res=180
)

## 9) P-scores (CSV 4 columnas)
rk <- netranks(nma, small.values="good")
.get_ps <- function(obj, trts){
  if (is.null(obj)) return(data.frame())
  if (is.numeric(obj) && is.atomic(obj) && is.null(dim(obj))) {
    ps <- as.numeric(obj); rn <- names(obj); if (is.null(rn) || any(rn=="")) rn <- trts
    rknum <- rank(-ps, ties.method="average")
    return(data.frame(Tratamiento=rn, Pscore=ps, Rank=rknum))
  }
  df <- as.data.frame(obj, stringsAsFactors=FALSE)
  rn <- rownames(df); if (is.null(rn) || any(rn=="")) rn <- trts
  cn <- tolower(gsub("[^a-z]", "", colnames(df)))
  idx_ps <- if (any(cn %in% c("pscore","pscorerandom","pscorecommon","p"))) which(cn %in%
c("pscore","pscorerandom","pscorecommon","p"))[1] else 1
  idx_rk <- if (any(cn %in% c("rank","rankrandom","rankcommon"))) which(cn %in%
c("rank","rankrandom","rankcommon"))[1] else NA_integer_
  ps <- as.numeric(df[[idx_ps]])
  rknum <- if (is.na(idx_rk)) rank(-ps, ties.method="average") else as.numeric(df[[idx_rk]])
  data.frame(Tratamiento=rn, Pscore=ps, Rank=rknum, row.names=NULL)
}
pscores <- merge(.get_ps(rk$ranking.random, nma$trts),
  .get_ps(rk$ranking.common, nma$trts),
  by="Tratamiento", all=TRUE,
  suffixes=c("_random","_common"))
if (!is.null(pscores$Rank_random)) pscores <- pscores[order(pscores$Rank_random), ]
colnames(pscores) <-
c("Tratamiento","Pscore_random","Rank_random","Pscore_common","Rank_common")
write.csv(pscores, file.path(outdir,"06_Pscores.csv"), row.names=FALSE)

## 10) Rankogram
set.seed(123)
plot_and_save(file.path(outdir,"06_rankogram.png"),
  rankogram(nma, small.values="good", n.iter=1000),
  width=1400, height=1100, res=170
)
sink(file.path(outdir,"06_rankogram.txt")); rankogram(nma, small.values="good", n.iter=1000); sink()

## 11) Funnel limpio (leyenda fuera)
lgd <- unique(paste(pairs$treat1, ":", pairs$treat2))
op <- par(no.readonly=TRUE)
par(fig=c(0, 0.72, 0, 1), mar=c(5,5,3,1), xpd=NA); funnel(nma, order=nma$trts, legend=FALSE)
par(fig=c(0.72, 1, 0, 1), mar=c(5,1,3,1), new=TRUE); plot.new(); legend("topleft", legend=lgd, bty="n",
cex=0.9)
```

```
par(op)
png(file.path(outdir,"07_funnel_clean.png"), width=1700, height=1100, res=170, fontsize=12)
op <- par(no.readonly=TRUE)
par(fig=c(0, 0.72, 0, 1), mar=c(5,5,3,1), xpd=NA); funnel(nma, order=nma$trts, legend=FALSE)
par(fig=c(0.72, 1, 0, 1), mar=c(5,1,3,1), new=TRUE); plot.new(); legend("topleft", legend=lgd, bty="n",
cex=0.9)
par(op); dev.off()

## 12) Heat map (+ nota si no aplica) y Q de Cochran
ok_heat <- TRUE
tryCatch({
  plot_and_save(file.path(outdir,"08_heat.png"), netheat(nma))
}, warning=function(w){ ok_heat <- FALSE },
  error=function(e){ ok_heat <- FALSE })
if (!ok_heat) writeLines(c(
  "Net heat plot no disponible:",
  "- La red puede no tener bucles cerrados suficientes."
), con=file.path(outdir,"08_heat_NOT_AVAILABLE.txt"))

sink(file.path(outdir,"09_Q_decomposition.txt")); print(decomp.design(nma)); sink()

## 13) README + sesión
cat(
  "Archivos generados:\n",
  "00_pairwise_dataset.csv\n",
  "01_NMA_summary.txt\n",
  "02_network.png\n",
  "03a_HR_vs_ADT_random_table.csv\n",
  "03b_forest_vs_ADT_order_auto.png\n",
  "04_league_table.txt / 04_league_table.csv\n",
  "05_SIDE_full.txt / 05_SIDE_forest_large.png\n",
  "06_Pscores.csv\n",
  "06_rankogram.txt / 06_rankogram.png\n",
  "07_funnel_clean.png\n",
  "08_heat.png o 08_heat_NOT_AVAILABLE.txt\n",
  "09_Q_decomposition.txt\n",
  file=file.path(outdir,"README_outputs.txt")
)
sink(file.path(outdir,"99_sessionInfo.txt")); print(sessionInfo()); sink()
cat("\nListo. Archivos en:\n", normalizePath(outdir), "\n")
```

### PREGUNTA 3 SOBREVIDA – ALTO

```
# =====
# NMA – OS (Burden = High) | Script autocontenido
# =====
run_nma_os_high_v3 <- function() {
  if (!requireNamespace("netmeta", quietly = TRUE))
    install.packages("netmeta", repos = "https://cloud.r-project.org")
  library(netmeta)

  op <- options(stringsAsFactors = FALSE); on.exit(options(op), add = TRUE)
  while (!is.null(dev.list())) dev.off()

  outdir <- paste0("NMA_OS_High_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  # ----- Datos (OS - High) -----
  raw_txt <- "
```

```

ID_art\tEstudio\tAutor\tAño\tTratamiento\tN_por_brazo\tHR_OS\tIC_Inf\tIC_Sup\tBurden
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT +
Bicalutamida\t404\t0.97\t0.7\t1.35\tHigh
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT + Flutamida\t409\tRef\tRef\tHigh
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT +
Bicalutamida\t404\t0.88\t0.69\t1.11\tHigh
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT + Flutamida\t409\tRef\tRef\tRef\tHigh
3\tKYUCOG-1401\tYokomizo A\t2024\tADT\t100\t1.17\t0.69\t1.96\tHigh
3\tKYUCOG-1401\tYokomizo A\t2024\tADT + Bicalutamida\t98\tRef\tRef\tRef\tHigh
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT +
Bicalutamida\t404\t0.87\t0.72\t1.05\tHigh
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT + Flutamida\t409\tRef\tRef\tRef\tHigh
7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Enzalutamida\t36\t0.31\t0.13\t0.74\tHigh
7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Bicalutamida\t35\tRef\tRef\tRef\tHigh
10\tLATITUDE\tFizazi K\t2017\tADT + Abiraterona\t597\t0.62\t0.51\t0.76\tHigh
10\tLATITUDE\tFizazi K\t2017\tADT\t602\tRef\tRef\tRef\tHigh
11\tPEACE-1\tFizazi K\t2022\tADT + Abiraterona\t583\t0.82\t0.69\t0.98\tHigh
11\tPEACE-1\tFizazi K\t2022\tADT\t589\tRef\tRef\tRef\tHigh
13\tSTAMPEDE - Arm G\tJames ND\t2017\tADT + Abiraterona\t501\t0.61\t0.49\t0.75\tHigh
13\tSTAMPEDE - Arm G\tJames ND\t2017\tADT\t502\tRef\tRef\tRef\tHigh
"

dat <- read.table(text = raw_txt, header = TRUE, sep = "\t",
  quote = "", check.names = FALSE)
dat$Tratamiento <- gsub(" +", " ", trimws(dat$Tratamiento))

# ----- Helpers compartidos -----
isRef <- function(x) {
  x <- trimws(as.character(x))
  suppressWarnings(is.na(as.numeric(x))) | toupper(x) %in% c("REF", "REFERENCE")
}
build_pairs <- function(df, outcome_col = "HR_OS", lcl_col = "IC_Inf", ucl_col = "IC_Sup") {
  do.call(rbind, lapply(split(df, df$ID_art), function(d) {
    base <- d[isRef(d[[outcome_col]]), , drop = FALSE]
    if (!nrow(base)) return(NULL)
    base_trt <- base$Tratamiento[1]
    d <- d[!isRef(d[[outcome_col]]), , drop = FALSE]
    if (!nrow(d)) return(NULL)
    data.frame(
      studlab = paste(d$Estudio, d$Año),
      treat1 = d$Tratamiento,
      treat2 = base_trt,
      TE = log(as.numeric(d[[outcome_col]])),
      seTE = (log(as.numeric(d[[ucl_col]])) - log(as.numeric(d[[lcl_col]]))) / (2*1.96),
      stringsAsFactors = FALSE
    )
  }))
}
order_by_hr_vs_ADT <- function(nma, ref.trt = "ADT") {
  nl <- netleague(nma, random = TRUE, common = FALSE)
  TEr <- nl$TE.random; SEr <- nl$seTE.random
  trts <- setdiff(nma$trts, ref.trt)
  rows <- lapply(trts, function(t) {
    r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
    te <- if (!is.na(r) && !is.na(c)) TEr[r, c] else NA_real_
    se <- if (!is.na(r) && !is.na(c)) SEr[r, c] else NA_real_
    if (is.na(te)) {
      r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
      if (!is.na(r2) && !is.na(c2) && !is.na(TEr[r2, c2])) { te <- -TEr[r2, c2]; se <- SEr[r2, c2] }
    }
  })
  data.frame(Tratamiento = t,
    HR = exp(te),
    LCL = exp(te - 1.96*se),

```

```

      UCL = exp(te + 1.96*se))
    })
    df <- do.call(rbind, rows)
    df <- df[order(df$HR, decreasing = FALSE), ]
    list(seq = c(df$Tratamiento, ref.trt), table = df)
  }
  toRankingDF <- function(x, trts) {
    if (is.null(x)) return(data.frame())
    if (is.atomic(x) && is.null(dim(x))) {
      rn <- names(x); if (is.null(rn) || any(rn=="")) rn <- trts
      return(data.frame(Tratamiento = rn,
        Pscore = as.numeric(x),
        Rank = rank(-as.numeric(x), ties.method="average")))
    }
    df <- as.data.frame(x)
    if (is.null(rownames(df)) || any(rownames(df)=="")) rownames(df) <- trts
    cn <- tolower(gsub("[^a-z]", "", colnames(df)))
    ip <- which(cn %in% c("pscore", "pscores", "p", "pscorerandom", "pscorecommon")); if (!length(ip)) ip <- 1
    ir <- which(cn %in% c("rank", "ranking", "rankrandom", "rankcommon"))
    P <- as.numeric(df[[ip[1]]]); R <- if (length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
    data.frame(Tratamiento = rownames(df), Pscore = P, Rank = R, row.names = NULL)
  }
  save_png <- function(file, w, h, res, fun) {
    png(file, width = w, height = h, res = res, pointsize = 11)
    fun(); dev.off()
  }

  # ----- Pairwise + conectividad -----
  pairs <- build_pairs(dat)
  write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names = FALSE)
  sink(file.path(outdir, "00_netconnection.txt"))
  print(netconnection(treat1 = pairs$treat1, treat2 = pairs$treat2, studlab = pairs$studlab))
  sink()

  # ----- NMA -----
  ref.trt <- "ADT"
  nma <- netmeta(TE = TE, seTE = seTE,
    treat1 = treat1, treat2 = treat2,
    studlab = studlab, data = pairs,
    sm = "HR", common = TRUE, random = TRUE,
    reference.group = ref.trt, method.tau = "REML",
    details = TRUE)
  sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits = 3); sink()

  # ----- Red -----
  par(mar = c(5,5,2,2))
  netgraph(nma, plastic = FALSE, multiarm = TRUE,
    thickness = "number.of.studies", number.of.studies = TRUE,
    cex.number = 0.9, points = TRUE, cex = 1.2)
  title(main = "Estructura de la red - OS (High)")
  save_png(file.path(outdir, "02_network.png"), 1600, 1200, 180, function(){
    par(mar = c(5,5,2,2))
    netgraph(nma, plastic = FALSE, multiarm = TRUE,
      thickness = "number.of.studies", number.of.studies = TRUE,
      cex.number = 0.9, points = TRUE, cex = 1.2)
    title(main = "Estructura de la red - OS (High)")
  })

  # ----- Forest (orden auto, dirección correcta) -----
  ord <- order_by_hr_vs_ADT(nma, ref.trt)
  write.csv(ord$table, file.path(outdir, "03_forest_order_source_table.csv"), row.names = FALSE)

```

```

par(mar = c(6,10,5,2))
forest(nma, ref = ref.trt, baseline = FALSE, seq = ord$seq,
      digits = 2, smlab = "HR (OS)",
      title = sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
save_png(file.path(outdir, "03_forest_vs_ADT_order_auto.png"), 1800, 1600, 180, function(){
  par(mar = c(6,10,5,2))
  forest(nma, ref = ref.trt, baseline = FALSE, seq = ord$seq,
        digits = 2, smlab = "HR (OS)",
        title = sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
})

# ----- League table -----
lt <- netleague(nma, random = TRUE, common = FALSE, digits = 2, bracket = "[", text = "HR")
sink(file.path(outdir, "04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir, "04_league_table.csv"))

# ----- SIDE + Q decomp -----
side <- netsplit(nma)
sink(file.path(outdir, "05_SIDE_full.txt")); print(side, digits = 3, show = "all"); sink()

par(mar = c(8,22,5,4))
forest(side, digits = 2, show = "all", cex = 0.9,
      title = "Directo vs Indirecto (SIDE) - OS (High)")
save_png(file.path(outdir, "05_SIDE_forest_large.png"), 2200, 2900, 180, function(){
  par(mar = c(8,22,5,4))
  forest(side, digits = 2, show = "all", cex = 0.9,
        title = "Directo vs Indirecto (SIDE) - OS (High)")
})
sink(file.path(outdir, "05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

# ----- Ranking / P-scores -----
rk <- netrank(nma, small.values = "good")
df_random <- toRankingDF(rk$ranking.random, nma$trts)
df_common <- toRankingDF(rk$ranking.common, nma$trts)
df_ps <- merge(transform(df_random, Pscore_random = Pscore, Rank_random =
Rank)[,c("Tratamiento", "Pscore_random", "Rank_random")],
  transform(df_common, Pscore_common = Pscore, Rank_common =
Rank)[,c("Tratamiento", "Pscore_common", "Rank_common")],
  by = "Tratamiento", all = TRUE)
df_ps <- df_ps[order(-df_ps$Pscore_random), ]
write.csv(df_ps, file.path(outdir, "06_pscores.csv"), row.names = FALSE)

# ----- Rankogram -----
rtxt <- capture.output(rankogram(nma, small.values = "good", n.iter = 1000))
title(main = "Rankogram - OS (High)")
writeLines(rtxt, file.path(outdir, "NMA_rankogram.txt"))
save_png(file.path(outdir, "NMA_rankogram.png"), 1600, 1200, 170, function(){
  rankogram(nma, small.values = "good", n.iter = 1000)
  title(main = "Rankogram - OS (High)")
})

# ----- Funnel (leyenda fuera) -----
labs_legend <- unique(paste(pairs$treat1, "vs", pairs$treat2))
save_png(file.path(outdir, "07_funnel_clean.png"), 1800, 1200, 170, function(){
  par(fig = c(0, 0.74, 0, 1), mar = c(5,5,3,1), xpd = NA)
  funnel(nma, order = ord$seq, legend = FALSE)
  title(main = "Funnel plot - OS (High)")
  par(fig = c(0.74, 1, 0, 1), mar = c(5,0,3,2), new = TRUE); plot.new()
  legend("left", legend = labs_legend, cex = 0.85, bty = "n")
})

# ----- Heat (puede no aplicar) -----

```



```
ok_heat <- TRUE
tryCatch({
  save_png(file.path(outdir,"08_heat.png"), 1600, 1200, 170, function(){
    par(mar = c(5,5,3,2)); netheat(nma); title(main = "Net heat - OS (High)")
  })
}, warning=function(w) ok_heat <- FALSE, error=function(e) ok_heat <- FALSE)
if (!ok_heat) {
  writeLines(c("Net heat plot no disponible:",
    "- La red no contiene bucles cerrados (estructura en estrella)."),
    file.path(outdir,"08_heat_NOT_AVAILABLE.txt"))
}

cat("\nArchivos en:", outdir, "\n"); print(list.files(outdir))
}

# ---- Ejecuta:
run_nma_os_high_v3()
```

### PREGUNTA 3 SOBREVIDA MIXTO

```
# Usa exactamente el mismo flujo que High, con la base Mixto
run_nma_os_mixto_v3 <- function() {
  if (!requireNamespace("netmeta", quietly = TRUE))
    install.packages("netmeta", repos = "https://cloud.r-project.org")
  library(netmeta)

  op <- options(stringsAsFactors = FALSE); on.exit(options(op), add = TRUE)
  while (!is.null(dev.list())) dev.off()

  outdir <- paste0("NMA_OS_Mixto_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  raw_txt <- "
Estudio\Autor\Año\Tratamiento\N_por_brazo\HR_OS\IC_Inf\IC_Sup\Burden
ARCHES\Armstrong AJ\2019\ADT + Enzalutamida\574\0.81\0.53\1.25\Mixto
ARCHES\Armstrong AJ\2019\ADT\576\Ref\Ref\Ref\Mixto
ENZAMET\Davis ID\2019\ADT + Enzalutamida\563\0.67\0.52\0.86\Mixto
ENZAMET\Davis ID\2019\ADT + Antiandrógeno Noesteroideo\562\Ref\Ref\Ref\Mixto
TITAN\Chi KN\2019\ADT + Apalutamida\525\0.67\0.51\0.89\Mixto
TITAN\Chi KN\2019\ADT\527\Ref\Ref\Ref\Mixto
"

  dat <- read.table(text = raw_txt, header = TRUE, sep = "\t", quote = "", check.names = FALSE)
  dat$Tratamiento <- gsub(" +", " ", trimws(dat$Tratamiento))
  dat$Burden <- trimws(dat$Burden)
  if (!"ID_art" %in% names(dat)) dat$ID_art <- as.integer(factor(paste(dat$Estudio, dat$Año, sep = "_")))

  # Helpers y funciones: copia exacta de las usadas en HIGH -----
  isRef <- function(x){ x <- trimws(as.character(x)); suppressWarnings(is.na(as.numeric(x))) | toupper(x)
  %in% c("REF", "REFERENCE") }
  build_pairs <- function(df, outcome_col="HR_OS", lcl_col="IC_Inf", ucl_col="IC_Sup"){
    do.call(rbind, lapply(split(df, df$ID_art), function(d){
      base <- d[isRef(d[[outcome_col]]), , drop=FALSE]; if (!nrow(base)) return(NULL)
      base_trt <- base$Tratamiento[1]
      d <- d[!isRef(d[[outcome_col]]), , drop=FALSE]; if (!nrow(d)) return(NULL)
      data.frame(studlab=paste(d$Estudio, d$Año),
        treat1=d$Tratamiento, treat2=base_trt,
        TE=log(as.numeric(d[[outcome_col]])),
        seTE=(log(as.numeric(d[[ucl_col]]))-log(as.numeric(d[[lcl_col]])))/(2*1.96))
    )))
  }
  order_by_hr_vs_ADT <- function(nma, ref.trt="ADT"){
    nl <- netleague(nma, random=TRUE, common=FALSE)
```

```

TEr <- nl$TE.random; SEr <- nl$seTE.random
trts <- setdiff(nma$trts, ref.trt)
rows <- lapply(trts, function(t){
  r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
  te <- if(!is.na(r)&&!is.na(c)) TEr[r,c] else NA_real_
  se <- if(!is.na(r)&&!is.na(c)) SEr[r,c] else NA_real_
  if (is.na(te)) { r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
    if(!is.na(r2)&&!is.na(c2)&&!is.na(TEr[r2,c2])){ te <- -TEr[r2,c2]; se <- SEr[r2,c2] } }
  data.frame(Tratamiento=t, HR=exp(te), LCL=exp(te-1.96*se), UCL=exp(te+1.96*se))
})
df <- do.call(rbind, rows); df <- df[order(df$HR), ]
list(seq=c(df$Tratamiento, ref.trt), table=df)
}
toRankingDF <- function(x, trts){
  if (is.null(x)) return(data.frame())
  if (is.atomic(x) && is.null(dim(x))){
    rn <- names(x); if(is.null(rn)||any(rn=="")) rn <- trts
    return(data.frame(Tratamiento=rn, Pscore=as.numeric(x), Rank=rank(-as.numeric(x),
ties.method="average")))
  }
  df <- as.data.frame(x); if(is.null(rownames(df))||any(rownames(df)=="")) rownames(df) <- trts
  cn <- tolower(gsub("[^a-z]", "", colnames(df))); ip <- which(cn %in%
c("pscore", "pscores", "p", "pscorerandom", "pscorecommon")); if(!length(ip)) ip <- 1
  ir <- which(cn %in% c("rank", "ranking", "rankrandom", "rankcommon"))
  P <- as.numeric(df[[ip[1]]]); R <- if(length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
  data.frame(Tratamiento=rownames(df), Pscore=P, Rank=R, row.names=NULL)
}
save_png <- function(file, w, h, res, fun){ png(file, width=w, height=h, res=res, pointsize=11); fun();
dev.off() }

# Pairwise + conectividad
pairs <- build_pairs(dat)
write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names=FALSE)
sink(file.path(outdir, "00_netconnection.txt")); print(netconnection(treat1=pairs$treat1,
treat2=pairs$treat2, studlab=pairs$studlab)); sink()

# NMA
ref.trt <- "ADT"
nma <- netmeta(TE=TE, seTE=seTE, treat1=treat1, treat2=treat2, studlab=studlab, data=pairs,
sm="HR", common=TRUE, random=TRUE, reference.group=ref.trt, method.tau="REML",
details=TRUE)
sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits=3); sink()

# Red
par(mar=c(5,5,2,2))
netgraph(nma, plastic=FALSE, multiarm=TRUE, thickness="number.of.studies", number.of.studies=TRUE,
cex.number=0.9, points=TRUE, cex=1.2)
title(main="Estructura de la red - OS (Mixto)")
save_png(file.path(outdir, "02_network.png"), 1600,1200,180, function(){
  par(mar=c(5,5,2,2))
  netgraph(nma, plastic=FALSE, multiarm=TRUE, thickness="number.of.studies", number.of.studies=TRUE,
cex.number=0.9, points=TRUE, cex=1.2)
  title(main="Estructura de la red - OS (Mixto)")
})

# Forest ordenado
ord <- order_by_hr_vs_ADT(nma, ref.trt)
write.csv(ord$table, file.path(outdir, "03_forest_order_source_table.csv"), row.names=FALSE)
par(mar=c(6,10,5,2))
forest(nma, ref=ref.trt, baseline=FALSE, seq=ord$seq, digits=2, smlab="HR (OS)",
title=sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
save_png(file.path(outdir, "03_forest_vs_ADT_order_auto.png"), 1800,1600,180, function(){

```

```

par(mar=c(6,10,5,2))
forest(nma, ref=ref.trt, baseline=FALSE, seq=ord$seq, digits=2, smlab="HR (OS)",
       title=sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
})

# League table
lt <- netleague(nma, random=TRUE, common=FALSE, digits=2, bracket="[" , text="HR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

# SIDE + Q
side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits=3, show="all"); sink()
par(mar=c(8,22,5,4))
forest(side, digits=2, show="all", cex=0.9, title="Directo vs Indirecto (SIDE) – OS (Mixto)")
save_png(file.path(outdir,"05_SIDE_forest_large.png"), 2200,2600,180, function(){
  par(mar=c(8,22,5,4))
  forest(side, digits=2, show="all", cex=0.9, title="Directo vs Indirecto (SIDE) – OS (Mixto)")
})
sink(file.path(outdir,"05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

# Ranking / P-scores
rk <- netrank(nma, small.values="good")
df_random <- toRankingDF(rk$ranking.random, nma$trts)
df_common <- toRankingDF(rk$ranking.common, nma$trts)
df_ps <- merge(transform(df_random, Pscore_random=Pscore,
Rank_random=Rank)[,c("Tratamiento", "Pscore_random", "Rank_random")],
               transform(df_common, Pscore_common=Pscore,
Rank_common=Rank)[,c("Tratamiento", "Pscore_common", "Rank_common")],
               by="Tratamiento", all=TRUE)
df_ps <- df_ps[order(-df_ps$Pscore_random), ]
write.csv(df_ps, file.path(outdir,"06_pscores.csv"), row.names=FALSE)

# Rankogram
rtxt <- capture.output(rankogram(nma, small.values="good", n.iter=1000))
title(main="Rankogram – OS (Mixto)")
writeLines(rtxt, file.path(outdir,"NMA_rankogram.txt"))
save_png(file.path(outdir,"NMA_rankogram.png"), 1600,1200,170, function(){
  rankogram(nma, small.values="good", n.iter=1000); title(main="Rankogram – OS (Mixto)")
})

# Funnel (leyenda fuera)
labs_legend <- unique(paste(pairs$treat1,"vs",pairs$treat2))
save_png(file.path(outdir,"07_funnel_clean.png"), 1800,1200,170, function(){
  par(fig=c(0,0.74,0,1), mar=c(5,5,3,1), xpd=NA)
  funnel(nma, order=ord$seq, legend=FALSE)
  title(main="Funnel plot – OS (Mixto)")
  par(fig=c(0.74,1,0,1), mar=c(5,0,3,2), new=TRUE); plot.new()
  legend("left", legend=labs_legend, cex=0.85, bty="n")
})

# Heat
ok_heat <- TRUE
tryCatch({
  save_png(file.path(outdir,"08_heat.png"), 1600,1200,170, function(){
    par(mar=c(5,5,3,2)); netheat(nma); title(main="Net heat – OS (Mixto)")
  })
}, warning=function(w) ok_heat <-< FALSE, error=function(e) ok_heat <-< FALSE)
if (!ok_heat) {
  writeLines(c("Net heat plot no disponible:",
               "- La red no contiene bucles cerrados (estructura en estrella)."),
            file.path(outdir,"08_heat_NOT_AVAILABLE.txt"))
}

```

```
}

cat("\nArchivos en:", outdir, "\n"); print(list.files(outdir))
}

# ---- Ejecuta:
run_nma_os_mixto_v3()
```

### PREGUNTA 3 SOBREVIDA LIBRE DE PROGRESIÓN

```
## =====
## NMA - PFS (HR_PFS) | consola + archivos | orden automático
## =====

if (!requireNamespace("netmeta", quietly = TRUE))
  install.packages("netmeta", repos = "https://cloud.r-project.org")
library(netmeta)
graphics.off(); layout(1); par(mfrow=c(1,1), mar=c(5.1,4.1,4.1,2.1))

outdir <- "NMA_output_PFS_full"
dir.create(outdir, showWarnings = FALSE)

plot_and_save <- function(file, expr,
                          width=1400, height=1000, res=170, pointsize=12,
                          mar=c(5.1,4.1,4.1,2.1)) {
  op <- par(no.readonly = TRUE); on.exit(par(op), add = TRUE)
  layout(1); par(mfrow=c(1,1), mar=mar)
  eval.parent(substitute(expr))
  png(file, width=width, height=height, res=res, pointsize=pointsize)
  layout(1); par(mfrow=c(1,1), mar=mar)
  eval.parent(substitute(expr))
  dev.off()
}

raw_txt <- "
ID_art\tEstudio\tAutor\tAño\tTratamiento\tN_por_brazo\tHR_PFS\tIC_Inf\tIC_Sup
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT + Bicalutamida\t404\t0.75\t0.61\t0.92
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT + Flutamida\t409\tRef\tRef\tRef
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT + Bicalutamida\t404\t0.9\t0.75\t1.08
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT + Flutamida\t409\tRef\tRef\tRef
3\tKYUCOG-1401\tYokomizo A\t2024\tADT\t100\t1.4\t1.01\t1.95
3\tKYUCOG-1401\tYokomizo A\t2024\tADT + Bicalutamida\t98\tRef\tRef\tRef
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT + Bicalutamida\t404\t0.93\t0.79\t1.1
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT + Flutamida\t409\tRef\tRef\tRef
7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Enzalutamida\t36\t0.15\t0.05\t0.47
7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Bicalutamida\t35\tRef\tRef\tRef
8\tARCHES\tArmstrong AJ\t2019\tADT + Enzalutamida\t574\t0.39\t0.3\t0.5
8\tARCHES\tArmstrong AJ\t2019\tADT\t576\tRef\tRef\tRef
9\tENZAMET\tDavis ID\t2019\tADT + Enzalutamida\t563\t0.4\t0.33\t0.49
9\tENZAMET\tDavis ID\t2019\tADT + Antiandr geno Noesteroideo\t562\tRef\tRef\tRef
10\tLATITUDE\tFizazi K\t2017\tADT + Abiraterona\t597\t0.47\t0.39\t0.55
10\tLATITUDE\tFizazi K\t2017\tADT\t602\tRef\tRef\tRef
11\tPEACE-1\tFizazi K\t2022\tADT + Abiraterona\t583\t0.54\t0.41\t0.71
11\tPEACE-1\tFizazi K\t2022\tADT\t589\tRef\tRef\tRef
12\tTITAN\tChi KN\t2019\tADT + Apalutamida\t525\t0.48\t0.39\t0.6
12\tTITAN\tChi KN\t2019\tADT\t527\tRef\tRef\tRef
13\tSTAMPEDE - Arm G\tJames ND\t2017\tADT + Abiraterona\t501\t0.29\t0.25\t0.34
13\tSTAMPEDE - Arm G\tJames ND\t2017\tADT\t502\tRef\tRef\tRef
"

dat0 <- read.table(text=raw_txt, header=TRUE, sep="\t", quote="",
                  check.names=FALSE, stringsAsFactors=FALSE)
```

```
std_trt <- function(x) { x <- trimws(x); x <- sub("^ADT \\((Degarelix\\))$", "ADT", x); x }
dat0$Tratamiento <- std_trt(dat0$Tratamiento)

isRef <- function(x) is.na(suppressWarnings(as.numeric(x))) |
  toupper(trimws(x)) %in% c("REF", "REFERENCE")

pairs <- do.call(rbind, lapply(split(dat0, dat0$ID_art), function(d) {
  base <- d[isRef(d$HR_PFS), , drop=FALSE]
  if (nrow(base) == 0) stop("Sin 'Ref' en ID_art=", d$ID_art[1])
  base_trt <- base$Tratamiento[1]
  d <- d[!isRef(d$HR_PFS), , drop=FALSE]
  if (!nrow(d)) return(NULL)
  data.frame(
    studlab = paste(d$Estudio, d$Año),
    treat1 = d$Tratamiento,
    treat2 = base_trt,
    TE = log(as.numeric(d$HR_PFS)),
    seTE = (log(as.numeric(d$IC_Sup)) - log(as.numeric(d$IC_Inf))) / (2*1.96),
    stringsAsFactors = FALSE
  )
}))
write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names=FALSE)

ref.trt <- "ADT"
nma <- netmeta(TE=TE, seTE=seTE,
  treat1=treat1, treat2=treat2,
  studlab=studlab, data=pairs,
  sm="HR", common=TRUE, random=TRUE,
  reference.group=ref.trt, method.tau="REML",
  details=TRUE)
sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits=3); sink()

plot_and_save(file.path(outdir, "02_network.png"),
  netgraph(nma, plastic=FALSE, multiarm=TRUE,
    thickness="number.of.studies", number.of.studies=TRUE,
    cex.number=0.9, points=TRUE, cex=1.2)
)

compute_hr_vs_ref <- function(nma, ref.trt) {
  te <- nma$TE.random; se <- nma$seTE.random
  trts <- setdiff(nma$trts, ref.trt)
  get_from_matrix <- function(te_mat, se_mat, ref, t) {
    r <- match(ref, rownames(te_mat)); c <- match(t, colnames(te_mat))
    te <- if (!is.na(r)&&!is.na(c)) te_mat[r,c] else NA_real_
    se <- if (!is.na(r)&&!is.na(c)) se_mat[r,c] else NA_real_
    if (is.na(te)||is.na(se)) {
      r2 <- match(t, rownames(te_mat)); c2 <- match(ref, colnames(te_mat))
      if (!is.na(r2)&&!is.na(c2)&&!is.na(te_mat[r2,c2])) { te <- -te_mat[r2,c2]; se <- se_mat[r2,c2] }
    }
    list(te=te, se=se)
  }
  if (is.numeric(te) && is.null(dim(te)) && length(te)>0 && length(te)<=length(trts)+2) {
    nm <- names(te); if (is.null(nm)||length(nm)==0) nm <- trts
    se_vec <- if (!is.null(names(se)) && length(names(se))) se[nm] else se[seq_along(nm)]
    te_num <- as.numeric(te[seq_along(nm)]); se_num <- as.numeric(se_vec)
    return(data.frame(Tratamiento=nm, HR=exp(te_num),
      LCL=exp(te_num-1.96*se_num), UCL=exp(te_num+1.96*se_num)))
  }
  if (is.matrix(te) && is.matrix(se)) {
    rows <- lapply(trts, function(t){
      z <- get_from_matrix(te, se, ref.trt, t)
      data.frame(Tratamiento=t, HR=exp(z$te),
```

```

      LCL=exp(z$te-1.96*z$se), UCL=exp(z$te+1.96*z$se))
    }); return(do.call(rbind, rows))
  }
  nl <- netleague(nma, random=TRUE, common=FALSE)
  TEr <- nl$TE.random; SEr <- nl$seTE.random
  rows <- lapply(trts, function(t){
    r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
    te1 <- if (!is.na(r)&&!is.na(c)) TEr[r,c] else NA_real_
    se1 <- if (!is.na(r)&&!is.na(c)) SEr[r,c] else NA_real_
    if (is.na(te1)||is.na(se1)) {
      r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
      if (!is.na(r2)&&!is.na(c2) && !is.na(TEr[r2,c2])) { te1 <- -TEr[r2,c2]; se1 <- SEr[r2,c2] }
    }
    data.frame(Tratamiento=t, HR=exp(te1), LCL=exp(te1-1.96*se1), UCL=exp(te1+1.96*se1))
  })
  do.call(rbind, rows)
}
hr_tab <- compute_hr_vs_ref(nma, ref.trt)
hr_tab <- hr_tab[order(hr_tab$HR, decreasing=FALSE), ]
write.csv(hr_tab, file.path(outdir,"03a_HR_vs_ADT_random_table.csv"), row.names=FALSE)

orden_auto <- c(hr_tab$Tratamiento, ref.trt)
plot_and_save(file.path(outdir,"03b_forest_vs_ADT_order_auto.png"),
  forest(nma, ref=ref.trt, seq=orden_auto,
    baseline=FALSE, drop=TRUE, digits=2, smlab="HR (PFS)",
    title="Comparison: other treatments vs 'ADT' (Random Effects)",
    width=1800, height=1600, res=180
  )
)

lt <- netleague(nma, random=TRUE, common=FALSE, digits=2, bracket="[" , text="HR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits=3, show="all"); sink()
sdf <- tryCatch(as.data.frame(side), error=function(e) NULL)
ncomp <- if (!is.null(sdf)) nrow(sdf) else 30L
height_px <- max(3000, 700 + 90*ncomp)
plot_and_save(file.path(outdir,"05_SIDE_forest_large.png"),
  { op <- par(mar=c(10,22,6,6)); on.exit(par(op), add=TRUE)
    forest(side, digits=2, show="all", cex=0.9,
      title="Comparación directa vs indirecta (SIDE) – HR (PFS)" },
  width=2500, height=height_px, res=180
)

rk <- netranks(nma, small.values="good")
.get_ps <- function(obj, trts){
  if (is.null(obj)) return(data.frame())
  if (is.numeric(obj) && is.atomic(obj) && is.null(dim(obj))) {
    ps <- as.numeric(obj); rn <- names(obj); if (is.null(rn)||any(rn=="")) rn <- trts
    rknum <- rank(-ps, ties.method="average")
    return(data.frame(Tratamiento=rn, Pscore=ps, Rank=rknum))
  }
  df <- as.data.frame(obj, stringsAsFactors=FALSE)
  rn <- rownames(df); if (is.null(rn) || any(rn=="")) rn <- trts
  cn <- tolower(gsub("[^a-z]", "", colnames(df)))
  idx_ps <- if (any(cn %in% c("pscore", "pscorerandom", "pscorecommon", "p"))) which(cn %in%
c("pscore", "pscorerandom", "pscorecommon", "p"))[1] else 1
  idx_rk <- if (any(cn %in% c("rank", "rankrandom", "rankcommon"))) which(cn %in%
c("rank", "rankrandom", "rankcommon"))[1] else NA_integer_
  ps <- as.numeric(df[[idx_ps]])
  rknum <- if (is.na(idx_rk)) rank(-ps, ties.method="average") else as.numeric(df[[idx_rk]])
}

```

```

data.frame(Tratamiento=rn, Pscore=ps, Rank=rknum, row.names=NULL)
}
pscores <- merge(.get_ps(rk$ranking.random, nma$trts),
  .get_ps(rk$ranking.common, nma$trts),
  by="Tratamiento", all=TRUE,
  suffixes=c("_random", "_common"))
if (!is.null(pscores$Rank_random)) pscores <- pscores[order(pscores$Rank_random), ]
colnames(pscores) <-
c("Tratamiento", "Pscore_random", "Rank_random", "Pscore_common", "Rank_common")
write.csv(pscores, file.path(outdir, "06_Pscores.csv"), row.names=FALSE)

set.seed(123)
plot_and_save(file.path(outdir, "06_rankogram.png"),
  rankogram(nma, small.values="good", n.iter=1000),
  width=1400, height=1100, res=170
)
sink(file.path(outdir, "06_rankogram.txt")); rankogram(nma, small.values="good", n.iter=1000); sink()

lgd <- unique(paste(pairs$treat1, ":", pairs$treat2))
op <- par(no.readonly=TRUE)
par(fig=c(0, 0.72, 0, 1), mar=c(5,5,3,1), xpd=NA); funnel(nma, order=nma$trts, legend=FALSE)
par(fig=c(0.72, 1, 0, 1), mar=c(5,1,3,1), new=TRUE); plot.new(); legend("topleft", legend=lgd, bty="n",
  cex=0.9)
par(op)
png(file.path(outdir, "07_funnel_clean.png"), width=1700, height=1100, res=170, pointsize=12)
op <- par(no.readonly=TRUE)
par(fig=c(0, 0.72, 0, 1), mar=c(5,5,3,1), xpd=NA); funnel(nma, order=nma$trts, legend=FALSE)
par(fig=c(0.72, 1, 0, 1), mar=c(5,1,3,1), new=TRUE); plot.new(); legend("topleft", legend=lgd, bty="n",
  cex=0.9)
par(op); dev.off()

ok_heat <- TRUE
tryCatch({
  plot_and_save(file.path(outdir, "08_heat.png"), netheat(nma))
}, warning=function(w){ ok_heat <- FALSE },
  error=function(e){ ok_heat <- FALSE })
if (!ok_heat) writeLines(c(
  "Net heat plot no disponible:",
  "- La red puede no tener bucles cerrados suficientes."
), con=file.path(outdir, "08_heat_NOT_AVAILABLE.txt"))

sink(file.path(outdir, "09_Q_decomposition.txt")); print(decomp.design(nma)); sink()

cat(
  "Archivos generados:\n",
  "00_pairwise_dataset.csv\n",
  "01_NMA_summary.txt\n",
  "02_network.png\n",
  "03a_HR_vs_ADT_random_table.csv\n",
  "03b_forest_vs_ADT_order_auto.png\n",
  "04_league_table.txt / 04_league_table.csv\n",
  "05_SIDE_full.txt / 05_SIDE_forest_large.png\n",
  "06_Pscores.csv\n",
  "06_rankogram.txt / 06_rankogram.png\n",
  "07_funnel_clean.png\n",
  "08_heat.png o 08_heat_NOT_AVAILABLE.txt\n",
  "09_Q_decomposition.txt\n",
  file=file.path(outdir, "README_outputs.txt")
)
sink(file.path(outdir, "99_sessionInfo.txt")); print(sessionInfo()); sink()
cat("\nListo. Archivos en:\n", normalizePath(outdir), "\n")

```

### PREGUNTA 3 SOBREVIDA LIBRE DE PROGRESIÓN - ALTO#

```
=====
# NMA – PFS (Burden = High) | Script autocontenido
# Solo requiere: netmeta
# =====
run_nma_pfs_high <- function() {
  if (!requireNamespace("netmeta", quietly = TRUE))
    install.packages("netmeta", repos = "https://cloud.r-project.org")
  library(netmeta)

  op <- options(stringsAsFactors = FALSE); on.exit(options(op), add = TRUE)
  while (!is.null(dev.list())) dev.off()

  outdir <- paste0("NMA_PFS_High_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  # ----- Datos (PFS - High) -----
  raw_txt <- "
ID_art\tEstudio\tAutor\tAño\tTratamiento\tN_por_brazo\tHR_PFS\tIC_Inf\tIC_Sup\tBurden
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT +
Bicalutamida\t404\t0.75\t0.61\t0.92\tHigh
1\tCasodex Combination Study Group\tSchellhammer P\t1995\tADT + Flutamida\t409\tRef\tRef\tRef\tHigh
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT +
Bicalutamida\t404\t0.90\t0.75\t1.08\tHigh
2\tCasodex Combination Study Group\tSchellhammer P\t1996\tADT + Flutamida\t409\tRef\tRef\tRef\tHigh
3\tKYUCOG-1401\tYokomizo A\t2024\tADT\t100\t1.40\t1.01\t1.95\tHigh
3\tKYUCOG-1401\tYokomizo A\t2024\tADT + Bicalutamida\t98\tRef\tRef\tRef\tHigh
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT +
Bicalutamida\t404\t0.93\t0.79\t1.10\tHigh
5\tCasodex Combination Study Group\tSchellhammer PF\t1997\tADT + Flutamida\t409\tRef\tRef\tRef\tHigh
7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Enzalutamida\t36\t0.15\t0.05\t0.47\tHigh
7\tJAMA Oncol Trial\tVaishampayan U\t2021\tADT + Bicalutamida\t35\tRef\tRef\tRef\tHigh
10\tLATITUDE\tFizazi K\t2017\tADT + Abiraterona\t597\t0.47\t0.39\t0.55\tHigh
10\tLATITUDE\tFizazi K\t2017\tADT\t602\tRef\tRef\tRef\tHigh
11\tPEACE-1\tFizazi K\t2022\tADT + Abiraterona\t583\t0.54\t0.41\t0.71\tHigh
11\tPEACE-1\tFizazi K\t2022\tADT\t589\tRef\tRef\tRef\tHigh
13\tSTAMPEDE – Arm G\tJames ND\t2017\tADT + Abiraterona\t501\t0.29\t0.25\t0.34\tHigh
13\tSTAMPEDE – Arm G\tJames ND\t2017\tADT\t502\tRef\tRef\tRef\tHigh
"

  dat <- read.table(text = raw_txt, header = TRUE, sep = "\t",
    quote = "", check.names = FALSE)
  dat$Tratamiento <- gsub(" +", " ", trimws(dat$Tratamiento))

  # ----- Helpers -----
  isRef <- function(x) {
    x <- trimws(as.character(x))
    suppressWarnings(is.na(as.numeric(x))) | toupper(x) %in% c("REF", "REFERENCE")
  }
  build_pairs <- function(df, outcome_col = "HR_PFS", lcl_col = "IC_Inf", ucl_col = "IC_Sup") {
    do.call(rbind, lapply(split(df, df$ID_art), function(d) {
      base <- d[isRef(d[[outcome_col]]), , drop = FALSE]
      if (!nrow(base)) return(NULL)
      base_trt <- base$Tratamiento[1]
      d <- d[!isRef(d[[outcome_col]]), , drop = FALSE]
      if (!nrow(d)) return(NULL)
      data.frame(
        studlab = paste(d$Estudio, d$Año),
        treat1 = d$Tratamiento,
        treat2 = base_trt,
        TE = log(as.numeric(d[[outcome_col]])),
        seTE = (log(as.numeric(d[[ucl_col]])) - log(as.numeric(d[[lcl_col]]))) / (2*1.96),

```



```

    stringsAsFactors = FALSE
  )
})))
}
order_by_hr_vs_ADT <- function(nma, ref.trt = "ADT") {
  nl <- netleague(nma, random = TRUE, common = FALSE)
  TEr <- nl$TE.random; SEr <- nl$seTE.random
  trts <- setdiff(nma$trts, ref.trt)
  rows <- lapply(trts, function(t) {
    r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
    te <- if (!is.na(r) && !is.na(c)) TEr[r, c] else NA_real_
    se <- if (!is.na(r) && !is.na(c)) SEr[r, c] else NA_real_
    if (is.na(te)) {
      r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
      if (!is.na(r2) && !is.na(c2) && !is.na(TEr[r2, c2])) { te <- -TEr[r2, c2]; se <- SEr[r2, c2] }
    }
  })
  data.frame(Tratamiento = t,
    HR = exp(te),
    LCL = exp(te - 1.96*se),
    UCL = exp(te + 1.96*se))
})
df <- do.call(rbind, rows); df <- df[order(df$HR), ]
list(seq = c(df$Tratamiento, ref.trt), table = df)
}
toRankingDF <- function(x, trts){
  if (is.null(x)) return(data.frame())
  if (is.atomic(x) && is.null(dim(x))) {
    rn <- names(x); if(is.null(rn)||any(rn=="")) rn <- trts
    return(data.frame(Tratamiento=rn, Pscore=as.numeric(x),
      Rank=rank(-as.numeric(x), ties.method="average")))
  }
  df <- as.data.frame(x)
  if (is.null(rownames(df)) || any(rownames(df)=="")) rownames(df) <- trts
  cn <- tolower(gsub("[^a-z]", "", colnames(df)))
  ip <- which(cn %in% c("pscore", "pscores", "p", "pscorerandom", "pscorecommon")); if(!length(ip)) ip <- 1
  ir <- which(cn %in% c("rank", "ranking", "rankrandom", "rankcommon"))
  P <- as.numeric(df[[ip[1]]]); R <- if(length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
  data.frame(Tratamiento=rownames(df), Pscore=P, Rank=R, row.names=NULL)
}
save_png <- function(file, w, h, res, fun){
  png(file, width=w, height=h, res=res, pointsize=11); fun(); dev.off()
}

# ----- Pairwise + conectividad -----
pairs <- build_pairs(dat)
if (is.null(pairs) || !nrow(pairs)) stop("No se pudieron construir pares.")
write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names = FALSE)
sink(file.path(outdir, "00_netconnection.txt"))
print(netconnection(treat1 = pairs$treat1, treat2 = pairs$treat2, studlab = pairs$studlab))
sink()

# ----- NMA -----
ref.trt <- "ADT"
nma <- netmeta(TE = TE, seTE = seTE,
  treat1 = treat1, treat2 = treat2,
  studlab = studlab, data = pairs,
  sm = "HR", common = TRUE, random = TRUE,
  reference.group = ref.trt, method.tau = "REML",
  details = TRUE)
sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits = 3); sink()

# ----- Red -----

```

```

par(mar = c(5,5,2,2))
netgraph(nma, plastic = FALSE, multiarm = TRUE,
         thickness = "number.of.studies", number.of.studies = TRUE,
         cex.number = 0.9, points = TRUE, cex = 1.2)
title(main = "Estructura de la red - PFS (High)")
save_png(file.path(outdir,"02_network.png"), 1600, 1200, 180, function(){
  par(mar = c(5,5,2,2))
  netgraph(nma, plastic = FALSE, multiarm = TRUE,
           thickness = "number.of.studies", number.of.studies = TRUE,
           cex.number = 0.9, points = TRUE, cex = 1.2)
  title(main = "Estructura de la red - PFS (High)")
})

# ----- Forest (orden auto; tratamiento→ADT) -----
ord <- order_by_hr_vs_ADT(nma, ref.trt)
write.csv(ord$table, file.path(outdir,"03_forest_order_source_table.csv"), row.names = FALSE)

par(mar = c(6,10,5,2))
forest(nma, ref = ref.trt, baseline = FALSE, seq = ord$seq,
       digits = 2, smlab = "HR (PFS)",
       title = sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
save_png(file.path(outdir,"03_forest_vs_ADT_order_auto.png"), 1800, 1600, 180, function(){
  par(mar = c(6,10,5,2))
  forest(nma, ref = ref.trt, baseline = FALSE, seq = ord$seq,
        digits = 2, smlab = "HR (PFS)",
        title = sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
})

# ----- League table -----
lt <- netleague(nma, random = TRUE, common = FALSE, digits = 2, bracket = "[", text = "HR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

# ----- SIDE + Q decomp -----
side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits = 3, show = "all"); sink()
par(mar = c(8,22,5,4))
forest(side, digits = 2, show = "all", cex = 0.9,
       title = "Directo vs Indirecto (SIDE) - PFS (High)")
save_png(file.path(outdir,"05_SIDE_forest_large.png"), 2200, 2900, 180, function(){
  par(mar = c(8,22,5,4))
  forest(side, digits = 2, show = "all", cex = 0.9,
        title = "Directo vs Indirecto (SIDE) - PFS (High)")
})
sink(file.path(outdir,"05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

# ----- Ranking / P-scores -----
rk <- netrank(nma, small.values = "good")
df_random <- toRankingDF(rk$ranking.random, nma$trts)
df_common <- toRankingDF(rk$ranking.common, nma$trts)
df_ps <- merge(transform(df_random, Pscore_random = Pscore, Rank_random =
Rank)[,c("Tratamiento", "Pscore_random", "Rank_random")],
               transform(df_common, Pscore_common = Pscore, Rank_common =
Rank)[,c("Tratamiento", "Pscore_common", "Rank_common")],
               by = "Tratamiento", all = TRUE)
df_ps <- df_ps[order(-df_ps$Pscore_random), ]
write.csv(df_ps, file.path(outdir,"06_pscores.csv"), row.names = FALSE)

# -----

```

### PREGUNTA 3 SOBREVIDA LIBRE DE PROGRESIÓN – MIXTO

```
# =====
# NMA – PFS (Burden = Mixto) | Script autocontenido
# Solo requiere: netmeta
# =====
run_nma_pfs_mixto <- function() {
  if (!requireNamespace("netmeta", quietly = TRUE))
    install.packages("netmeta", repos = "https://cloud.r-project.org")
  library(netmeta)

  op <- options(stringsAsFactors = FALSE); on.exit(options(op), add = TRUE)
  while (!is.null(dev.list())) dev.off()

  outdir <- paste0("NMA_PFS_Mixto_", format(Sys.time(), "%Y%m%d_%H%M"))
  dir.create(outdir, showWarnings = FALSE)

  # ----- Datos (PFS - Mixto) -----
  raw_txt <- "
ID_art\tEstudio\tAutor\tAño\tTratamiento\tN_por_brazo\tHR_PFS\tIC_Inf\tIC_Sup\tBurden
8\tARCHES\tArmstrong AJ\t2019\tADT + Enzalutamida\t574\t0.39\t0.30\t0.50\tMixto
8\tARCHES\tArmstrong AJ\t2019\tADT\t576\tRef\tRef\tRef\tMixto
9\tENZAMET\tDavis ID\t2019\tADT + Enzalutamida\t563\t0.40\t0.33\t0.49\tMixto
9\tENZAMET\tDavis ID\t2019\tADT + Antiandrógeno Noesteroideo\t562\tRef\tRef\tRef\tMixto
12\tTITAN\tChi KN\t2019\tADT + Apalutamida\t525\t0.48\t0.39\t0.60\tMixto
12\tTITAN\tChi KN\t2019\tADT\t527\tRef\tRef\tRef\tMixto
"

  dat <- read.table(text = raw_txt, header = TRUE, sep = "\t",
    quote = "", check.names = FALSE)
  dat$Tratamiento <- gsub(" +", " ", trimws(dat$Tratamiento))

  # ----- Helpers -----
  isRef <- function(x) {
    x <- trimws(as.character(x))
    suppressWarnings(is.na(as.numeric(x))) | toupper(x) %in% c("REF", "REFERENCE")
  }
  build_pairs <- function(df, outcome_col = "HR_PFS", lcl_col = "IC_Inf", ucl_col = "IC_Sup") {
    do.call(rbind, lapply(split(df, df$ID_art), function(d) {
      base <- d[isRef(d[[outcome_col]]), , drop = FALSE]
      if (!nrow(base)) return(NULL)
      base_trt <- base$Tratamiento[1]
      d <- d[!isRef(d[[outcome_col]]), , drop = FALSE]
      if (!nrow(d)) return(NULL)
      data.frame(
        studlab = paste(d$Estudio, d$Año),
        treat1 = d$Tratamiento,
        treat2 = base_trt,
        TE = log(as.numeric(d[[outcome_col]])),
        seTE = (log(as.numeric(d[[ucl_col]])) - log(as.numeric(d[[lcl_col]]))) / (2*1.96),
        stringsAsFactors = FALSE
      )
    }))
  }
  order_by_hr_vs_ADT <- function(nma, ref.trt = "ADT") {
    nl <- netleague(nma, random = TRUE, common = FALSE)
    TEr <- nl$TE.random; SEr <- nl$seTE.random
    trts <- setdiff(nma$trts, ref.trt)
    rows <- lapply(trts, function(t) {
      r <- match(ref.trt, rownames(TEr)); c <- match(t, colnames(TEr))
      te <- if (!is.na(r) && !is.na(c)) TEr[r, c] else NA_real_
      se <- if (!is.na(r) && !is.na(c)) SEr[r, c] else NA_real_
    })
  }
}
```

```

if (is.na(te)) {
  r2 <- match(t, rownames(TEr)); c2 <- match(ref.trt, colnames(TEr))
  if (!is.na(r2) && !is.na(c2) && !is.na(TEr[r2, c2])) { te <- -TEr[r2, c2]; se <- SEr[r2, c2] }
}
data.frame(Tratamiento = t,
  HR = exp(te),
  LCL = exp(te - 1.96*se),
  UCL = exp(te + 1.96*se))
})
df <- do.call(rbind, rows); df <- df[order(df$HR), ]
list(seq = c(df$Tratamiento, ref.trt), table = df)
}
toRankingDF <- function(x, trts){
  if (is.null(x)) return(data.frame())
  if (is.atomic(x) && is.null(dim(x))){
    rn <- names(x); if(is.null(rn)||any(rn=="")) rn <- trts
    return(data.frame(Tratamiento=rn, Pscore=as.numeric(x),
      Rank=rank(-as.numeric(x), ties.method="average")))
  }
  df <- as.data.frame(x)
  if (is.null(rownames(df)) || any(rownames(df)=="")) rownames(df) <- trts
  cn <- tolower(gsub("[^a-z]", "", colnames(df)))
  ip <- which(cn %in% c("pscore", "pscores", "p", "pscorerandom", "pscorecommon")); if(!length(ip)) ip <- 1
  ir <- which(cn %in% c("rank", "ranking", "rankrandom", "rankcommon"))
  P <- as.numeric(df[[ip[1]]]); R <- if(length(ir)) as.numeric(df[[ir[1]]]) else rank(-P)
  data.frame(Tratamiento=rownames(df), Pscore=P, Rank=R, row.names=NULL)
}
save_png <- function(file, w, h, res, fun){
  png(file, width=w, height=h, res=res, pointsize=11); fun(); dev.off()
}

# ----- Pairwise + conectividad -----
pairs <- build_pairs(dat)
if (is.null(pairs) || !nrow(pairs)) stop("No se pudieron construir pares.")
write.csv(pairs, file.path(outdir, "00_pairwise_dataset.csv"), row.names = FALSE)
sink(file.path(outdir, "00_netconnection.txt"))
print(netconnection(treat1 = pairs$treat1, treat2 = pairs$treat2, studlab = pairs$studlab))
sink()

# ----- NMA -----
ref.trt <- "ADT"
nma <- netmeta(TE = TE, seTE = seTE,
  treat1 = treat1, treat2 = treat2,
  studlab = studlab, data = pairs,
  sm = "HR", common = TRUE, random = TRUE,
  reference.group = ref.trt, method.tau = "REML",
  details = TRUE)
sink(file.path(outdir, "01_NMA_summary.txt")); print(nma, digits = 3); sink()

# ----- Red -----
par(mar = c(5,5,2,2))
netgraph(nma, plastic = FALSE, multiarm = TRUE,
  thickness = "number.of.studies", number.of.studies = TRUE,
  cex.number = 0.9, points = TRUE, cex = 1.2)
title(main = "Estructura de la red - PFS (Mixto)")
save_png(file.path(outdir, "02_network.png"), 1600, 1200, 180, function(){
  par(mar = c(5,5,2,2))
  netgraph(nma, plastic = FALSE, multiarm = TRUE,
    thickness = "number.of.studies", number.of.studies = TRUE,
    cex.number = 0.9, points = TRUE, cex = 1.2)
  title(main = "Estructura de la red - PFS (Mixto)")
})

```

```
# ----- Forest (orden auto; tratamiento→ADT) -----
ord <- order_by_hr_vs_ADT(nma, ref.trt)
write.csv(ord$table, file.path(outdir,"03_forest_order_source_table.csv"), row.names = FALSE)

par(mar = c(6,10,5,2))
forest(nma, ref = ref.trt, baseline = FALSE, seq = ord$seq,
       digits = 2, smlab = "HR (PFS)",
       title = sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
save_png(file.path(outdir,"03_forest_vs_ADT_order_auto.png"), 1800, 1600, 180, function(){
  par(mar = c(6,10,5,2))
  forest(nma, ref = ref.trt, baseline = FALSE, seq = ord$seq,
        digits = 2, smlab = "HR (PFS)",
        title = sprintf("Comparison: other vs '%s' (Random Effects Model)", ref.trt))
})

# ----- League table -----
lt <- netleague(nma, random = TRUE, common = FALSE, digits = 2, bracket = "[", text = "HR")
sink(file.path(outdir,"04_league_table.txt")); print(lt); sink()
write.csv(as.matrix(lt), file.path(outdir,"04_league_table.csv"))

# ----- SIDE + Q decomp -----
side <- netsplit(nma)
sink(file.path(outdir,"05_SIDE_full.txt")); print(side, digits = 3, show = "all"); sink()
par(mar = c(8,22,5,4))
forest(side, digits = 2, show = "all", cex = 0.9,
       title = "Directo vs Indirecto (SIDE) - PFS (Mixto)")
save_png(file.path(outdir,"05_SIDE_forest_large.png"), 2200, 2900, 180, function(){
  par(mar = c(8,22,5,4))
  forest(side, digits = 2, show = "all", cex = 0.9,
        title = "Directo vs Indirecto (SIDE) - PFS (Mixto)")
})
sink(file.path(outdir,"05b_Q_decomposition.txt")); print(decomp.design(nma)); sink()

# ----- Ranking / P-scores -----
rk <- netranks(nma, small.values = "good")
df_random <- toRankingDF(rk$ranking.random, nma$trts)
df_common <- toRankingDF(rk$ranking.common, nma$trts)
df_ps <- merge(transform(df_random, Pscore_random = Pscore, Rank_random =
Rank)[,c("Tratamiento", "Pscore_random", "Rank_random")],
               transform(df_common, Pscore_common = Pscore, Rank_common =
Rank)[,c("Tratamiento", "Pscore_common", "Rank_common")],
               by = "Tratamiento", all = TRUE)
df_ps <- df_ps[order(-df_ps$Pscore_random), ]
write.csv(df_ps, file.path(outdir,"06_pscores.csv"), row.names = FALSE)

# ----- Rankogram -----
rtxt <- capture.output(rankogram(nma, small.values = "good", n.iter = 1000))
title(main = "Rankogram - PFS (Mixto)")
writeLines(rtxt, file.path(outdir,"NMA_rankogram.txt"))
save_png(file.path(outdir,"NMA_rankogram.png"), 1600, 1200, 170, function(){
  rankogram(nma, small.values = "good", n.iter = 1000)
  title(main = "Rankogram - PFS (Mixto)")
})

# ----- Funnel (leyenda fuera) -----
labs_legend <- unique(paste(pairs$treat1, "vs", pairs$treat2))
save_png(file.path(outdir,"07_funnel_clean.png"), 1800, 1200, 170, function(){
  par(fig = c(0, 0.74, 0, 1), mar = c(5,5,3,1), xpd = NA)
  funnel(nma, order = ord$seq, legend = FALSE)
  title(main = "Funnel plot - PFS (Mixto)")
  par(fig = c(0.74, 1, 0, 1), mar = c(5,0,3,2), new = TRUE); plot.new()
```

```

    legend("left", legend = labs_legend, cex = 0.85, bty = "n")
  })

# ----- Heat (si aplica) -----
ok_heat <- TRUE
tryCatch({
  save_png(file.path(outdir,"08_heat.png"), 1600, 1200, 170, function(){
    par(mar = c(5,5,3,2)); netheat(nma); title(main = "Net heat - PFS (Mixto)")
  })
}, warning=function(w) ok_heat <- FALSE, error=function(e) ok_heat <- FALSE)
if (!ok_heat) {
  writeLines(c("Net heat plot no disponible:",
    "- La red no contiene bucles cerrados (estructura en estrella)."),
    file.path(outdir,"08_heat_NOT_AVAILABLE.txt"))
}

cat("\nListo. Carpeta:", outdir, "\n"); print(list.files(outdir))

```

## Anexo K. Información de eventos adversos, vigilancia poscomercialización, y registros sanitarios de las tecnologías

Se presentan en el archivo suplementario titulado “Anexo K\_PT CA próstata Suplemento de tecnologías”

## Anexo L. Estrategias y proceso de búsqueda para la evaluación económica

### Anexo L.1. Estrategias de búsqueda para la evaluación económica

Las estrategias de búsquedas utilizadas en cada una de las bases electrónicas consultadas se presentan en

**Tabla L-1. Estrategia de búsqueda en Medline PubMed**

| Característica             | Reporte        |          |            |
|----------------------------|----------------|----------|------------|
| Tipo de búsqueda           | Nueva          |          |            |
| Bases de datos             | Medline PubMed |          |            |
| Plataforma                 | Elsevier       |          |            |
| Fecha de búsqueda          | 2025-07-11     |          |            |
| Rango de fecha de búsqueda | Ninguna        |          |            |
| Restricciones de lenguaje  | Ninguna        |          |            |
| Otros límites              |                |          |            |
| Estrategia de búsqueda     | Nº             | Búsqueda | Resultados |

| Característica | Reporte                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                | <p>1</p> <p>'lhrh agonist':ti,ab,kw OR 'goserelin':ti,ab,kw<br/> OR 'leuprolide':ti,ab,kw OR 'triptorelin':ti,ab,kw<br/> OR 'gnrh antagonist':ti,ab,kw OR 'degarelix':ti,ab,kw<br/> OR 'abiraterone':ti,ab,kw OR 'antiandrogen':ti,ab,kw<br/> OR 'bicalutamide':ti,ab,kw OR 'flutamide':ti,ab,kw<br/> OR 'androgen deprivation':ti,ab,kw<br/> OR 'enzalutamide':ti,ab,kw OR 'apalutamide':ti,ab,kw<br/> OR 'darolutamide':ti,ab,kw OR 'docetaxel':ti,ab,kw<br/> OR 'cabazitaxel':ti,ab,kw OR 'taxanes':ti,ab,kw<br/> OR 'ciproterone':ti,ab,kw OR 'olaparib':ti,ab,kw<br/> OR 'radium':ti,ab,kw OR 'lutetium':ti,ab,kw<br/> OR 'diethylstilbestrol':ti,ab,kw OR 'ra-223':ti,ab,kw<br/> OR 'lu-177':ti,ab,kw OR 'goserelin'/exp<br/> OR 'goserelin' OR 'leuprorelin'/exp<br/> OR 'leuprorelin' OR 'triptorelin'/exp<br/> OR 'triptorelin' OR 'gonadorelin'/exp<br/> OR 'gonadorelin' OR 'acetyl 2 naphthylalanyl 3<br/> chlorophenylalanyl 1 oxohexadecyl seryl 4<br/> aminophenylalanyl hydroorotyl 4 aminophenylalanyl<br/> carbamoil leucyl ilys prolyl alaninamide'/exp OR 'acetyl<br/> 2 naphthylalanyl 3 chlorophenylalanyl 1 oxohexadecyl<br/> seryl 4 aminophenylalanyl hydroorotyl 4<br/> aminophenylalanyl carbamoil leucyl ilys prolyl<br/> alaninamide' OR 'abiraterone acetate'/exp<br/> OR 'abiraterone acetate' OR 'abiraterone'/exp<br/> OR 'abiraterone' OR 'antiandrogen'/exp<br/> OR 'antiandrogen' OR 'bicalutamide'/exp<br/> OR 'bicalutamide' OR 'flutamide'/exp<br/> OR 'flutamide' OR 'enzalutamide'/exp<br/> OR 'enzalutamide' OR 'apalutamide'/exp<br/> OR 'apalutamide' OR 'darolutamide'/exp<br/> OR 'darolutamide' OR 'taxoid'/exp<br/> OR 'taxoid' OR 'docetaxel'/exp<br/> OR 'docetaxel' OR 'cabazitaxel'/exp<br/> OR 'cabazitaxel' OR 'olaparib'/exp<br/> OR 'olaparib' OR 'radium'/exp OR 'radium' OR 'radium-<br/> 233' OR 'radium ra 223 dichloride'/exp OR 'radium ra<br/> 223 dichloride' OR 'lutetium-177'/exp OR 'lutetium-<br/> 177' OR 'diethylstilbestrol'/exp<br/> OR 'diethylstilbestrol' OR 'radiotherapy'/exp<br/> OR 'radiotherapy' OR 'zoladex':ti,ab,kw<br/> OR 'eligard':ti,ab,kw OR 'lupron':ti,ab,kw<br/> OR 'viadur':ti,ab,kw OR 'trelstar':ti,ab,kw<br/> OR 'firmagon':ti,ab,kw OR 'zytiga':ti,ab,kw<br/> OR 'orgovyx':ti,ab,kw OR 'plenaxis':ti,ab,kw<br/> OR 'casodex':ti,ab,kw OR 'eulexin':ti,ab,kw<br/> OR 'xtandi':ti,ab,kw OR 'erleada':ti,ab,kw<br/> OR 'nubeqa':ti,ab,kw OR 'androcur':ti,ab,kw<br/> OR 'jevtana':ti,ab,kw OR 'lynparza':ti,ab,kw<br/> OR 'distibene':ti,ab,kw OR 'honvol':ti,ab,kw<br/> OR 'stilbestrol':ti,ab,kw</p> <p>1337652</p> |



| Característica | Reporte |                                                                                                                                                                                                                                                                                                                                                                      |        |
|----------------|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
|                | 2       | 'prostatic' AND 'neoplasms' OR 'prostatic neoplasms' OR ('prostate' AND 'cancer') OR 'prostate cancer' OR 'prostate tumor'/exp OR 'prostatic neoplasms':ti,ab,kw OR 'neoplasm* prostatic':ti,ab,kw OR 'prostatic neoplasm*':ti,ab,kw OR 'neoplasm* prostate':ti,ab,kw OR 'prostate cancer':ti,ab,kw OR 'prostatic cancer*':ti,ab,kw OR 'cancer of prostate':ti,ab,kw | 402896 |
|                | 3       | #1 AND #2                                                                                                                                                                                                                                                                                                                                                            | 12662  |
|                | 4       | 'cost'/exp OR 'costs':ti,ab,kw OR 'cost effective*':ti,ab,kw                                                                                                                                                                                                                                                                                                         | 956166 |
|                | 5       | #3 AND #4                                                                                                                                                                                                                                                                                                                                                            | 3729   |
|                | 6       | 'cost effectiveness':ti,ab,kw OR 'health care cost'/de                                                                                                                                                                                                                                                                                                               | 362633 |
|                | 7       | #3 AND #6                                                                                                                                                                                                                                                                                                                                                            | 1895   |

**Tabla L-2. Estrategia de búsqueda en Embase**

| Característica             | Reporte    |          |            |
|----------------------------|------------|----------|------------|
| Tipo de búsqueda           | Nueva      |          |            |
| Bases de datos             | Embase     |          |            |
| Plataforma                 | Elsevier   |          |            |
| Fecha de búsqueda          | 2025-07-11 |          |            |
| Rango de fecha de búsqueda | Ninguna    |          |            |
| Restricciones de lenguaje  | Ninguna    |          |            |
| Otros límites              |            |          |            |
| Estrategia de búsqueda     | Nº         | Búsqueda | Resultados |

| Característica | Reporte                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                | <p>1</p> <p>'lhrh agonist':ti,ab,kw OR 'goserelin':ti,ab,kw<br/> OR 'leuprolide':ti,ab,kw OR 'triptorelin':ti,ab,kw<br/> OR 'gnrh antagonist':ti,ab,kw OR 'degarelix':ti,ab,kw<br/> OR 'abiraterone':ti,ab,kw OR 'antiandrogen':ti,ab,kw<br/> OR 'bicalutamide':ti,ab,kw OR 'flutamide':ti,ab,kw<br/> OR 'androgen deprivation':ti,ab,kw<br/> OR 'enzalutamide':ti,ab,kw OR 'apalutamide':ti,ab,kw<br/> OR 'darolutamide':ti,ab,kw OR 'docetaxel':ti,ab,kw<br/> OR 'cabazitaxel':ti,ab,kw OR 'taxanes':ti,ab,kw<br/> OR 'ciproterone':ti,ab,kw OR 'olaparib':ti,ab,kw<br/> OR 'radium':ti,ab,kw OR 'lutetium':ti,ab,kw<br/> OR 'diethylstilbestrol':ti,ab,kw OR 'ra-223':ti,ab,kw<br/> OR 'lu-177':ti,ab,kw OR 'goserelin'/exp<br/> OR 'goserelin' OR 'leuprorelin'/exp<br/> OR 'leuprorelin' OR 'triptorelin'/exp<br/> OR 'triptorelin' OR 'gonadorelin'/exp<br/> OR 'gonadorelin' OR 'acetyl 2 naphthylalanyl 3<br/> chlorophenylalanyl 1 oxohexadecyl seryl 4<br/> aminophenylalanyl hydroorotyl 4 aminophenylalanyl<br/> carbamoyl leucyl ilys prolyl alaninamide'/exp OR 'acetyl<br/> 2 naphthylalanyl 3 chlorophenylalanyl 1 oxohexadecyl<br/> seryl 4 aminophenylalanyl hydroorotyl 4<br/> aminophenylalanyl carbamoyl leucyl ilys prolyl<br/> alaninamide' OR 'abiraterone acetate'/exp<br/> OR 'abiraterone acetate' OR 'abiraterone'/exp<br/> OR 'abiraterone' OR 'antiandrogen'/exp<br/> OR 'antiandrogen' OR 'bicalutamide'/exp<br/> OR 'bicalutamide' OR 'flutamide'/exp<br/> OR 'flutamide' OR 'enzalutamide'/exp<br/> OR 'enzalutamide' OR 'apalutamide'/exp<br/> OR 'apalutamide' OR 'darolutamide'/exp<br/> OR 'darolutamide' OR 'taxoid'/exp<br/> OR 'taxoid' OR 'docetaxel'/exp<br/> OR 'docetaxel' OR 'cabazitaxel'/exp<br/> OR 'cabazitaxel' OR 'olaparib'/exp<br/> OR 'olaparib' OR 'radium'/exp OR 'radium' OR 'radium-<br/> 233' OR 'radium ra 223 dichloride'/exp OR 'radium ra<br/> 223 dichloride' OR 'lutetium-177'/exp OR 'lutetium-<br/> 177' OR 'diethylstilbestrol'/exp<br/> OR 'diethylstilbestrol' OR 'radiotherapy'/exp<br/> OR 'radiotherapy' OR 'zoladex':ti,ab,kw<br/> OR 'eligard':ti,ab,kw OR 'lupron':ti,ab,kw<br/> OR 'viadur':ti,ab,kw OR 'trelstar':ti,ab,kw<br/> OR 'firmagon':ti,ab,kw OR 'zytiga':ti,ab,kw<br/> OR 'orgovyx':ti,ab,kw OR 'plenaxis':ti,ab,kw<br/> OR 'casodex':ti,ab,kw OR 'eulexin':ti,ab,kw<br/> OR 'xtandi':ti,ab,kw OR 'erleada':ti,ab,kw<br/> OR 'nubeqa':ti,ab,kw OR 'androcure':ti,ab,kw<br/> OR 'jevtana':ti,ab,kw OR 'lynparza':ti,ab,kw<br/> OR 'distibene':ti,ab,kw OR 'honvol':ti,ab,kw<br/> OR 'stilbestrol':ti,ab,kw</p> <p>1337652</p> |

| Característica | Reporte |                                                                                                                                                                                                                                                                                                                                                                      |        |
|----------------|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
|                | 2       | 'prostatic' AND 'neoplasms' OR 'prostatic neoplasms' OR ('prostate' AND 'cancer') OR 'prostate cancer' OR 'prostate tumor'/exp OR 'prostatic neoplasms':ti,ab,kw OR 'neoplasm* prostatic':ti,ab,kw OR 'prostatic neoplasm*':ti,ab,kw OR 'neoplasm* prostate':ti,ab,kw OR 'prostate cancer':ti,ab,kw OR 'prostatic cancer*':ti,ab,kw OR 'cancer of prostate':ti,ab,kw | 402896 |
|                | 3       | #1 AND #2                                                                                                                                                                                                                                                                                                                                                            | 12662  |
|                | 4       | 'cost'/exp OR 'costs':ti,ab,kw OR 'cost effective*':ti,ab,kw                                                                                                                                                                                                                                                                                                         | 956166 |
|                | 5       | #3 AND #4                                                                                                                                                                                                                                                                                                                                                            | 3729   |
|                | 6       | 'cost effectiveness':ti,ab,kw OR 'health care cost'/de                                                                                                                                                                                                                                                                                                               | 362633 |
|                | 7       | #3 AND #6                                                                                                                                                                                                                                                                                                                                                            | 1895   |

**Tabla L-3. Estrategia de búsqueda en LILACS Plus**

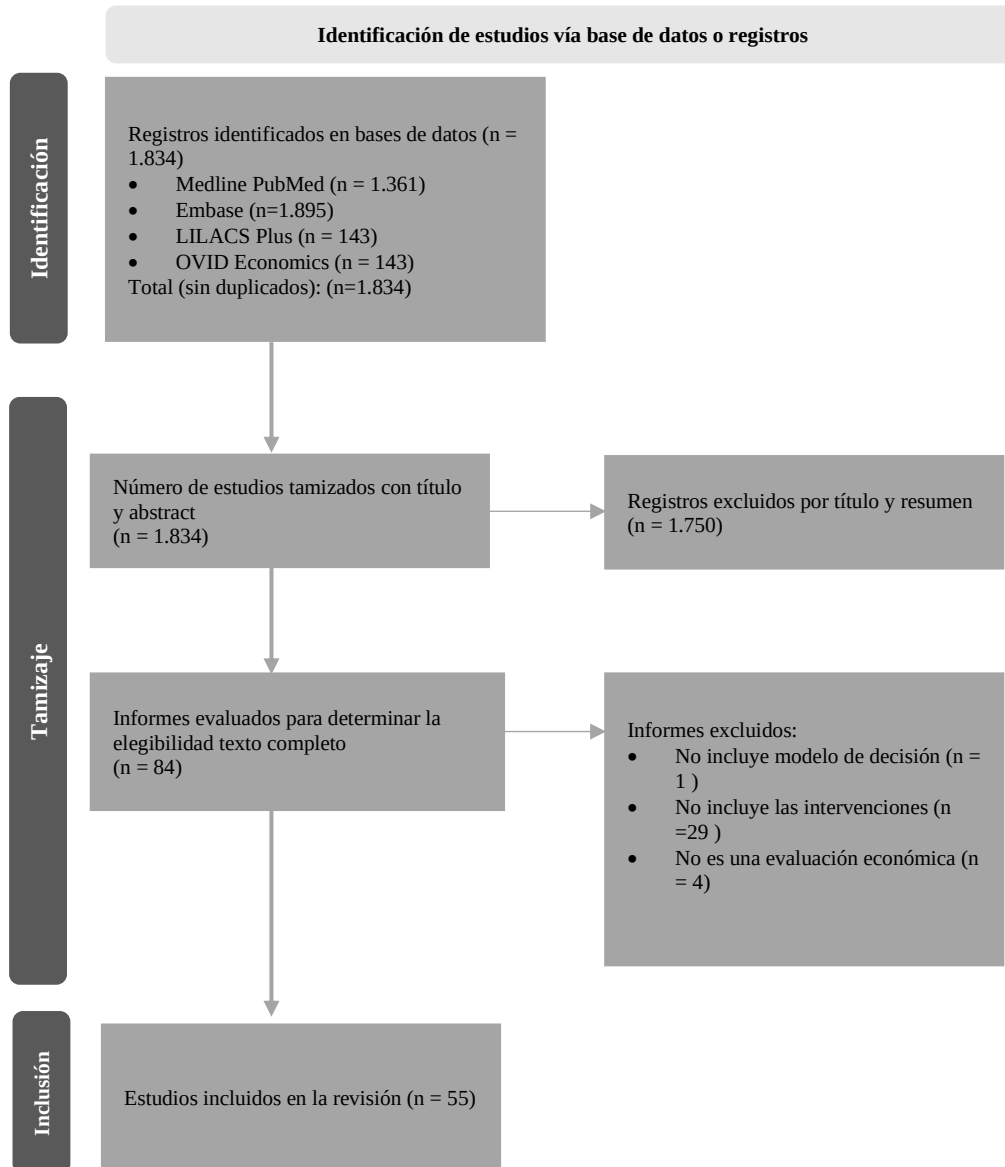
| Característica             | Reporte    |                                                                                                                                                                                                                                                                                                                                            |            |
|----------------------------|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Tipo de búsqueda           | Nueva      |                                                                                                                                                                                                                                                                                                                                            |            |
| Bases de datos             | Embase     |                                                                                                                                                                                                                                                                                                                                            |            |
| Plataforma                 | Elsevier   |                                                                                                                                                                                                                                                                                                                                            |            |
| Fecha de búsqueda          | 2025-07-11 |                                                                                                                                                                                                                                                                                                                                            |            |
| Rango de fecha de búsqueda | Ninguna    |                                                                                                                                                                                                                                                                                                                                            |            |
| Restricciones de lenguaje  | Ninguna    |                                                                                                                                                                                                                                                                                                                                            |            |
| Otros límites              |            |                                                                                                                                                                                                                                                                                                                                            |            |
| Estrategia de búsqueda     | Nº         | Búsqueda                                                                                                                                                                                                                                                                                                                                   | Resultados |
|                            | 1          | ((Goserelina) OR (Leuprolida) OR (Triptorelin) OR (Degarelix) OR (abiraterona) OR (bicalutamida) OR (flutamida) OR (Enzalutamida) OR (apalutamida) OR (Darolutamida) OR (Docetaxel) OR (Ciproterona) OR (Cabazitaxel) OR (Olaparib) OR (radio) OR (Lutecio) OR (dietilbestrol))                                                            | 20.033     |
|                            | 2          | ((prostate) AND (cancer)) OR ((prosta*) AND (neop*))                                                                                                                                                                                                                                                                                       | 15.332     |
|                            | 3          | ((Goserelina) OR (Leuprolida) OR (Triptorelin) OR (Degarelix) OR (abiraterona) OR (bicalutamida) OR (flutamida) OR (Enzalutamida) OR (apalutamida) OR (Darolutamida) OR (Docetaxel) OR (Ciproterona) OR (Cabazitaxel) OR (Olaparib) OR (radio) OR (Lutecio) OR (dietilbestrol)) AND (((prostate) AND (cancer)) OR ((prosta*) AND (neop*))) | 539        |
|                            | 4          | (health_economic_evaluation) OR (health_technology_assessment) OR (evaluación económica) OR (pharmacoeconomics) OR (farmacoeconomía)                                                                                                                                                                                                       | 9.101      |

|  |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |    |  |
|--|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|--|
|  | 5 | ((Goserelina) OR (Leuprolida) OR (Triptorelin) OR (Degarelix) OR (abiraterona) OR (bicalutamida) OR (flutamida) OR (Enzalutamida) OR (apalutamida) OR (Darolutamida) OR (Docetaxel) OR (Ciproterona) OR (Cabazitaxel) OR (Olaparib) OR (radio) OR (Lutecio) OR (dietilbestrol)) AND (((prostate) AND (cancer)) OR ((prosta*) AND (neop*))) AND (health_economic_evaluation) OR (health_technology_assessment) OR (evaluación económica) OR (pharmacoeconomics) OR (farmacoeconomía) | 66 |  |
|--|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|--|

**Tabla L-4. Estrategia de búsqueda en OVID Economics**

| Característica             | Reporte        |                                                                                                                                                                                                                                                                                                       |            |
|----------------------------|----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Tipo de búsqueda           | Nueva          |                                                                                                                                                                                                                                                                                                       |            |
| Bases de datos             | OVID Economics |                                                                                                                                                                                                                                                                                                       |            |
| Plataforma                 | Elsevier       |                                                                                                                                                                                                                                                                                                       |            |
| Fecha de búsqueda          | 2025-07-11     |                                                                                                                                                                                                                                                                                                       |            |
| Rango de fecha de búsqueda | Ninguna        |                                                                                                                                                                                                                                                                                                       |            |
| Restricciones de lenguaje  | Ninguna        |                                                                                                                                                                                                                                                                                                       |            |
| Otros límites              |                |                                                                                                                                                                                                                                                                                                       |            |
| Estrategia de búsqueda     | Nº             | Búsqueda                                                                                                                                                                                                                                                                                              | Resultados |
|                            | 1              | exp Prostate cancer/ or Prostat* canc*.mp. or exp Prostatic neoplasms/ or neoplasm* prostatic*.mp                                                                                                                                                                                                     | 18626      |
|                            | 2              | (Goserelin or Leuprolide or Leuproreline or degarelix or abiraterone or antiandrog* or bicalutamide or flutamide or androg* depriv* or Enzalutamide or apalutamide or Darolutamide or taxanes or docetaxel or cabazitaxel or ciproterone or olaparib or radium or lutetium or Diethylstilbestrol).mp. | 18020      |
|                            | 3              | 1 and 4                                                                                                                                                                                                                                                                                               | 6.504      |
|                            | 4              | exp "costs and cost analysis"/ or costs.tw. or cost effective?.tw.                                                                                                                                                                                                                                    | 71.688     |
|                            | 5              | 5 and 6                                                                                                                                                                                                                                                                                               | 143        |

## Anexo L.2. PRISMA proceso de búsqueda para la evaluación económica



## Anexo M. Resultados previos pregunta 4

### Anexo M.1 Resultados efectividad y seguridad previos pregunta 4

Pregunta 4. ¿En pacientes con diagnóstico de cáncer de próstata metastásico resistente a castración, cuál es la efectividad y seguridad de la terapia farmacológica combinada de segunda línea?

- **Resultados de efectividad**

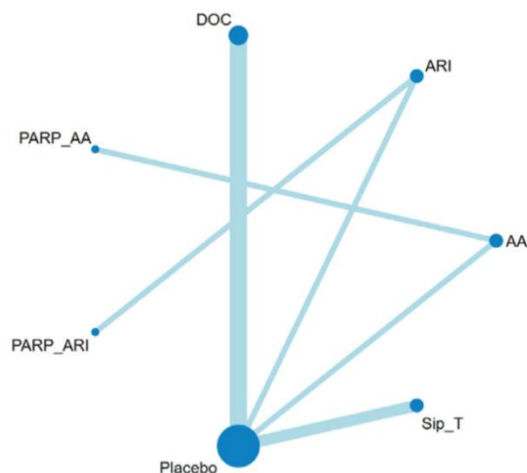
Para esta pregunta, la revisión sistemática con metaanálisis en red de Jiang et al. (1) publicada en 2005, presenta resultados agrupados de las diferentes tecnologías en esta población. Para ello, los autores realizaron una búsqueda sistemática en 2024 y seleccionaron 24 ensayos clínicos en pacientes con diagnóstico de CP metastásico resistente a castración sin mutaciones conocidas en HRR, que afecta significativamente el manejo; y con manejo con las diferentes tecnologías como primera y segunda línea de tratamiento.

- **Supervivencia global**

- ✓ **Manejo de primera línea**

La revisión encontró que las diferentes tecnologías tenían un efecto terapéutico significativo en el aumento de la supervivencia global. Sin embargo, solo docetaxel tenía un efecto terapéutico clínicamente significativo (HR: 0,77; IC95%: 0,57-1). La figura M-1 describe la red eM-2 describe los resultados de las comparaciones y la certeza en la evidencia.

**Figura M-1. Red de comparaciones indirectas para supervivencia global en primera línea**



Tomada de Jiang et al. (1)

En esta red los autores identificaron otras tecnologías no seleccionadas según la metodología de este lineamiento como Sipuleucel-T (Sip\_T) y Talazoparib + Enzalutamida (PARP\_ARI). Las tecnologías incluidas en este lineamiento que fueron incluidas en el estudio de Jiang et al. son: docetaxel (DOC), inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA).

**Tabla M-1. Tabla de ligas de comparaciones indirectas para supervivencia global en primera línea**

| AA                   |                      |                      |                      |                      |                   |         |
|----------------------|----------------------|----------------------|----------------------|----------------------|-------------------|---------|
| 1.06<br>[0.54, 2.06] | ARI                  |                      |                      |                      |                   |         |
| 0.97<br>[0.57, 1.73] | 0.92<br>[0.54, 1.62] | DOC                  |                      |                      |                   |         |
| 1.16<br>[0.71, 1.92] | 1.10<br>[0.48, 2.52] | 1.20<br>[0.55, 2.47] | PARP_AA              |                      |                   |         |
| 1.19<br>[0.52, 2.73] | 1.12<br>[0.68, 1.83] | 1.22<br>[0.57, 2.49] | 1.02<br>[0.39, 2.71] | PARP_ARI             |                   |         |
| 1.05<br>[0.6, 1.99]  | 1<br>[0.57, 1.87]    | 1.09<br>[0.69, 1.74] | 0.91<br>[0.43, 2.06] | 0.89<br>[0.42, 1.99] | Sip_T             |         |
| 0.75<br>[0.47, 1.21] | 0.71<br>[0.44, 1.13] | 0.77<br>[0.57, 1]    | 0.65<br>[0.32, 1.29] | 0.63<br>[0.32, 1.25] | 0.71<br>[0.48, 1] | Placebo |

Para leer la comparación se debe leer la columna más grande (intervención) vs. la más pequeña (referencia). Tomada de Jiang et al. (1)

En esta red los autores identificaron otras tecnologías no seleccionadas según la metodología de este lineamiento como Sipuleucel-T (Sip\_T) y Talazoparib + Enzalutamida (PARP\_ARI). Las tecnologías incluidas en este lineamiento que fueron incluidas en el estudio de Jiang et al. son: docetaxel (DOC), inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA).



**Tabla M-2. Resultados de las comparaciones indirectas y valoración de la certeza de la evidencia para supervivencia global en primera línea. Tomada y adaptada de Jiang et al. (36)**

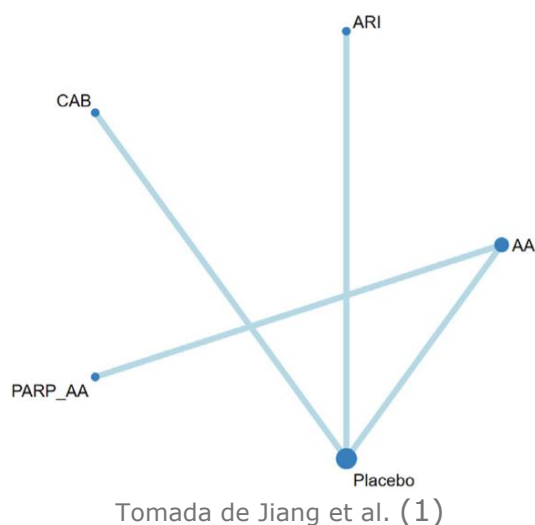
| Comparación |          | Evidencia indirecta  |                       |                 |                                       | Evidencia de la red |                                       |                      |              |                                                        |                     |               |
|-------------|----------|----------------------|-----------------------|-----------------|---------------------------------------|---------------------|---------------------------------------|----------------------|--------------|--------------------------------------------------------|---------------------|---------------|
| Brazo 1     | Brazo 2  | HR IC 95%            | Calificación Más Baja | Intransitividad | Comparación indirecta sin imprecisión | Imprecisión         | Comparación indirecta sin imprecisión | HR IC 95%            | Incoherencia | Calificación más alta de evidencia directa o indirecta | Imprecisión del MAR | Puntaje final |
| AA          | ARI      | 1.06<br>[0.54, 2.06] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.06<br>[0.54, 2.06] | No           | Mod                                                    | Serious             | Bajo          |
| AA          | DOC      | 0.97<br>[0.57, 1.73] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.97<br>[0.57, 1.73] | No           | Mod                                                    | Serious             | Bajo          |
| AA          | PARP_AA  | 1.16<br>[0.71, 1.92] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.16<br>[0.71, 1.92] | No           | Mod                                                    | Serious             | Bajo          |
| AA          | PARP_ARI | 1.19<br>[0.52, 2.73] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.19<br>[0.52, 2.73] | No           | Mod                                                    | Serious             | Bajo          |
| AA          | Placebo  | 0.75<br>[0.47, 1.21] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.75<br>[0.47, 1.21] | No           | Mod                                                    | Serious             | Bajo          |
| AA          | Sip-T    | 1.05<br>[0.6, 1.99]  | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.05<br>[0.6, 1.99]  | No           | Mod                                                    | Serious             | Bajo          |
| ARI         | DOC      | 0.92<br>[0.54, 1.62] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.92<br>[0.54, 1.62] | No           | Mod                                                    | Serious             | Bajo          |
| ARI         | PARP_AA  | 1.1<br>[0.48, 2.52]  | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.1<br>[0.48, 2.52]  | No           | Mod                                                    | Serious             | Bajo          |
| ARI         | PARP_ARI | 1.12<br>[0.68, 1.83] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.12<br>[0.68, 1.83] | No           | Mod                                                    | Serious             | Bajo          |
| ARI         | Placebo  | 0.71<br>[0.44, 1.13] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.71<br>[0.44, 1.13] | No           | Mod                                                    | Serious             | Bajo          |
| ARI         | Sip-T    | 1<br>[0.57, 1.87]    | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.00<br>[0.57, 1.87] | No           | Mod                                                    | Serious             | Bajo          |
| DOC         | PARP_AA  | 1.2<br>[0.55, 2.47]  | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.2<br>[0.55, 2.47]  | No           | Mod                                                    | Serious             | Bajo          |
| DOC         | PARP_ARI | 1.22<br>[0.57, 2.49] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.22<br>[0.57, 2.49] | No           | Mod                                                    | Serious             | Bajo          |
| DOC         | Placebo  | 0.77<br>[0.57, 1]    | Mod                   | No              | Alto                                  | No                  | Alto                                  | 0.77<br>[0.57, 1.00] | No           | Alto                                                   | No                  | Alto          |
| DOC         | Sip-T    | 1.09<br>[0.69, 1.74] | Alto                  | No              | Mod                                   | Serious             | Mod                                   | 1.09<br>[0.69, 1.74] | No           | Alto                                                   | Serious             | Bajo          |
| PARP_AA     | PARP_ARI | 1.02<br>[0.39, 2.71] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 1.02<br>[0.39, 2.71] | No           | Mod                                                    | Serious             | Bajo          |
| PARP_AA     | Placebo  | 0.65<br>[0.32, 1.29] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.65<br>[0.32, 1.29] | No           | Mod                                                    | Serious             | Bajo          |

| Comparación |         | Evidencia indirecta  |                       |                 |                                       | Evidencia de la red |                                       |                      |              |                                                        |                     |               |
|-------------|---------|----------------------|-----------------------|-----------------|---------------------------------------|---------------------|---------------------------------------|----------------------|--------------|--------------------------------------------------------|---------------------|---------------|
| Brazo 1     | Brazo 2 | HR IC 95%            | Calificación Más Baja | Intransitividad | Comparación indirecta sin imprecisión | Imprecisión         | Comparación indirecta sin imprecisión | HR IC 95%            | Incoherencia | Calificación más alta de evidencia directa o indirecta | Imprecisión del MAR | Puntaje final |
| PARP_AA     | Sip-T   | 0.91<br>[0.43, 2.06] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.91<br>[0.43, 2.06] | No           | Mod                                                    | Serious             | Bajo          |
| PARP_ARI    | Placebo | 0.63<br>[0.32, 1.25] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.63<br>[0.32, 1.25] | No           | Mod                                                    | Serious             | Bajo          |
| PARP_ARI    | Sip-T   | 0.89<br>[0.42, 1.99] | Mod                   | No              | Mod                                   | Serious             | Bajo                                  | 0.89<br>[0.42, 1.99] | No           | Mod                                                    | Serious             | Bajo          |
| Sip-T       | Placebo | 0.71<br>[0.48, 1.00] | Mod                   | No              | Alto                                  | No                  | Alto                                  | 0.71<br>[0.48, 1.00] | No           | Alto                                                   | No                  | Alto          |

## ✓ Manejo de segunda línea

Para el manejo de segunda línea, los investigadores no encontraron ninguna tecnología que cumpliera con una diferencia clínicamente significativa. La figura M-2 describe la red encontrada por los investigadores y la tabla M-3 los estimados combinados de las comparaciones indirectas, la tabla M-4 describe los resultados de las comparaciones y la certeza en la evidencia.

**Figura M-2. Red de comparaciones indirectas para supervivencia global en primera línea.**



Las tecnologías incluidas en este lineamiento que fueron incluidas en el estudio de Jiang et al. son: cabazitaxel (CAB), inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA).

**Tabla M-3. Tabla de ligas de comparaciones indirectas para supervivencia global en segunda línea.**

| AA                   |                      |                      |                      |         |
|----------------------|----------------------|----------------------|----------------------|---------|
| 1.03<br>[0.44, 2.4]  | ARI                  |                      |                      |         |
| 0.93<br>[0.4, 2.16]  | 0.9<br>[0.39, 2.09]  | CAB                  |                      |         |
| 1.02<br>[0.51, 2.03] | 0.99<br>[0.33, 2.93] | 1.09<br>[0.37, 3.24] | PARP_AA              |         |
| 0.65<br>[0.36, 1.19] | 0.63<br>[0.35, 1.15] | 0.70<br>[0.39, 1.28] | 0.64<br>[0.26, 1.59] | Placebo |

Para leer la comparación se debe leer la columna más grande (intervención) vs. la más pequeña (referencia). Tomada de Jiang et al. (1)

Las tecnologías incluidas en este lineamiento que fueron incluidas en este estudio son: cabazitaxel (CAB), inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA).

**Tabla M-4. Resultados de las comparaciones indirectas y valoración de la certeza de la evidencia para supervivencia global en segunda línea.**

| Brazo 1 | Brazo 2 | HR IC 95%            | Calificación Más Baja | Intransitividad | Comparación indirecta sin imprecisión | Imprecisión | Comparación indirecta sin imprecisión | HR IC 95%            | Incoherencia | Calificación más alta de evidencia directa o indirecta | Impresión del MAR | Puntaje final |
|---------|---------|----------------------|-----------------------|-----------------|---------------------------------------|-------------|---------------------------------------|----------------------|--------------|--------------------------------------------------------|-------------------|---------------|
| AA      | ARI     | 1.03<br>[0.44, 2.4]  | Mod                   | No              | Mod                                   | Serio       | Bajo                                  | 1.03<br>[0.44, 2.4]  | No           | Mod                                                    | Serio             | Bajo          |
| AA      | CAB     | 0.93<br>[0.4, 2.16]  | Mod                   | No              | Mod                                   | Serio       | Bajo                                  | 0.95<br>[0.4, 2.18]  | No           | Mod                                                    | Serio             | Bajo          |
| AA      | PARP_AA | NR                   | NR                    | NR              | NR                                    | NR          | NR                                    | 1.02<br>[0.3, 3.03]  | No           | Mod                                                    | Serio             | Bajo          |
| AA      | Placebo | NR                   | NR                    | NR              | NR                                    | NR          | NR                                    | 0.65<br>[0.36, 1.19] | No           | Mod                                                    | Serio             | Bajo          |
| ABI     | CAB     | 0.9<br>[0.39, 2.09]  | Mod                   | No              | Mod                                   | Serio       | Bajo                                  | 0.9<br>[0.39, 2.09]  | No           | Mod                                                    | Serio             | Bajo          |
| ABI     | PARP_AA | 0.99<br>[0.31, 3.15] | Mod                   | No              | Mod                                   | Serio       | Bajo                                  | 0.99<br>[0.31, 2.93] | No           | Mod                                                    | Serio             | Bajo          |
| ABI     | Placebo | NR                   | NR                    | NR              | NR                                    | NR          | NR                                    | 0.63<br>[0.33, 1.15] | No           | Mod                                                    | Serio             | Bajo          |
| CAB     | PARP_AA | 1.09<br>[0.37, 3.24] | Mod                   | No              | Mod                                   | Serio       | Bajo                                  | 1.09<br>[0.37, 3.24] | No           | Mod                                                    | Serio             | Bajo          |
| CAB     | Placebo | NR                   | NR                    | NR              | NR                                    | NR          | NR                                    | 0.7<br>[0.38, 1.28]  | No           | Mod                                                    | Serio             | Bajo          |

|         |         |                      |     |    |     |       |      |                      |    |     |       |      |
|---------|---------|----------------------|-----|----|-----|-------|------|----------------------|----|-----|-------|------|
| PARP_AA | Placebo | 0.64<br>[0.26, 1.59] | Mod | No | Mod | Serio | Bajo | 0.64<br>[0.26, 1.59] | No | Mod | Serio | Bajo |
|---------|---------|----------------------|-----|----|-----|-------|------|----------------------|----|-----|-------|------|

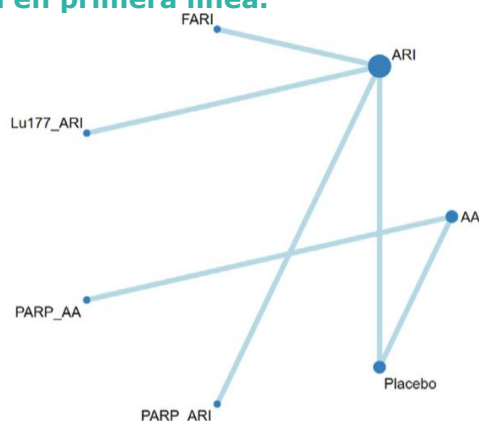
Tomada de Jiang et al. (1)

## ○ Supervivencia libre de progresión radiológica (rPFS)

### ✓ Manejo de primera línea

Los autores del estudio encontraron que las tecnologías evaluadas tenían un efecto no significativo en este desenlace. La figura M-3 presenta la red de comparaciones indirectas y la M-5 la tabla de ligas para estas comparaciones. La tabla M-6 describe las comparaciones individuales y la certeza de la evidencia.

**Figura M-3. Red de comparaciones indirectas para supervivencia libre de progresión radiológica en primera línea.**



Tomada de Jiang et al. (1)

En esta red los autores identificaron otra tecnología no seleccionada según la metodología de este lineamiento como Talazoparib + Enzalutamida (PARP\_ARI). Las tecnologías incluidas en este lineamiento que fueron incluidas en este estudio son: inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA), Lutecio-177 + inhibidores de receptor de andrógenos de segunda generación (Lu177\_ARI) e inhibidores de receptor de andrógenos de primera generación (FARI).

**Tabla M-5. Tabla de ligas de comparaciones indirectas para supervivencia libre de progresión radiológica en primera línea.**

|                       |                      |      |
|-----------------------|----------------------|------|
| AA                    |                      |      |
| 2.26<br>[0.12, 43.64] | ARI                  |      |
| 1.15<br>[0.03, 43.66] | 0.51<br>[0.06, 4.19] | FARI |

|                        |                       |                       |                       |                        |                      |                |
|------------------------|-----------------------|-----------------------|-----------------------|------------------------|----------------------|----------------|
| 3.33<br>[0.09, 127.54] | 1.47<br>[0.18, 12.37] | 2.89<br>[0.15, 57.13] | <b>Lu177 ARI</b>      |                        |                      |                |
| 1.52<br>[0.19, 12.16]  | 0.67<br>[0.02, 24.55] | 1.32<br>[0.02, 85.53] | 0.45<br>[0.01, 29.87] | <b>PARP_AA</b>         |                      |                |
| 3.61<br>[0.1, 134.28]  | 1.6<br>[0.2, 12.8]    | 3.14<br>[0.16, 60.77] | 1.08<br>[0.05, 21.28] | 2.39<br>[0.04, 154.45] | <b>PARP_ARI</b>      |                |
| 0.43<br>[0.05, 3.51]   | 0.19<br>[0.02, 1.96]  | 0.37<br>[0.02, 7.4]   | 0.13<br>[0.01, 2.91]  | 0.28<br>[0.01, 5.5]    | 0.12<br>[0.01, 2.35] | <b>Placebo</b> |

Para leer la comparación se debe leer la columna más grande (intervención) vs. la más pequeña (referencia). Tomada de Jiang et al. (1)

Las tecnologías incluidas en este lineamiento que fueron incluidas en este estudio son: inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA), Lutecio-177 + inhibidores de receptor de andrógenos de segunda generación (Lu177\_ARI) e inhibidores de receptor de andrógenos de primera generación (FARI).

**Tabla M-6. Resultados de las comparaciones indirectas y valoración de la certeza de la evidencia para supervivencia libre de progresión radiológica en primera línea.**

| Comparación |           | Evidencia indirecta    |                       |                 |                                     | Evidencia de la red |                                     |                        |              |                                                        |                   |               |
|-------------|-----------|------------------------|-----------------------|-----------------|-------------------------------------|---------------------|-------------------------------------|------------------------|--------------|--------------------------------------------------------|-------------------|---------------|
| Brazo 1     | Brazo 2   | HR IC 95%              | Calificación Más Baja | Intransitividad | Comparación indirecta sin impresión | Impresión           | Comparación indirecta sin impresión | HR IC 95%              | Incoherencia | Calificación más alta de evidencia directa o indirecta | Impresión del MAR | Puntaje final |
| AA          | ABI       | 2.27<br>[0.12, 43.64]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 2.27<br>[0.12, 43.64]  | No           | Mod                                                    | Muy serio         | Bajo          |
| AA          | FARP      | 1.15<br>[0.03, 43.66]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 1.15<br>[0.03, 43.66]  | No           | Mod                                                    | Muy serio         | Bajo          |
| AA          | Lu177_ARI | 3.33<br>[0.09, 127.54] | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 3.33<br>[0.09, 127.54] | No           | Mod                                                    | Muy serio         | Bajo          |
| AA          | PARP_AA   | NR<br>[NR, NR]         | NR                    | NR              | NR                                  | NR                  | NR                                  | 1.52<br>[0.19, 12.16]  | No           | Mod                                                    | Muy serio         | Bajo          |
| AA          | PARP_ARI  | 3.61<br>[0.1, 134.28]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 3.61<br>[0.1, 134.28]  | No           | Mod                                                    | Muy serio         | Bajo          |
| AA          | Placebo   | NR                     | NR                    | NR              | NR                                  | NR                  | NR                                  | 0.43<br>[0.05, 3.51]   | No           | Mod                                                    | Serious           | Bajo          |
| ARI         | FARI      | NR                     | NR                    | NR              | NR                                  | NR                  | NR                                  | 0.51<br>[0.06, 4.19]   | No           | Mod                                                    | Serious           | Bajo          |
| ARI         | Lu177_ARI | NR                     | NR                    | NR              | NR                                  | NR                  | NR                                  | 1.47<br>[0.18, 12.37]  | No           | Mod                                                    | Muy serio         | Bajo          |
| ARI         | PARP_AA   | 0.67<br>[0.02, 24.55]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 0.67<br>[0.02, 24.55]  | No           | Mod                                                    | Muy serio         | Bajo          |
| ARI         | PARP_ARI  | NR                     | NR                    | NR              | NR                                  | NR                  | NR                                  | 1.6<br>[0.2, 12.8]     | No           | Mod                                                    | Muy serio         | Bajo          |
| ARI         | Placebo   | NR                     | NR                    | NR              | NR                                  | NR                  | NR                                  | 0.19<br>[0.02, 1.56]   | No           | Mod                                                    | Serious           | Bajo          |
| FARI        | Lu177_ARI | 2.89<br>[0.15, 57.13]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 2.89<br>[0.15, 57.13]  | No           | Mod                                                    | Muy serio         | Bajo          |
| FARI        | PARP_AA   | 1.32<br>[0.02, 85.53]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 1.32<br>[0.02, 85.53]  | No           | Mod                                                    | Muy serio         | Bajo          |
| FARI        | PARP_ARI  | 3.14<br>[0.16, 60.77]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 3.14<br>[0.16, 60.77]  | No           | Mod                                                    | Muy serio         | Bajo          |
| FARI        | Placebo   | 0.37<br>[0.02, 7.4]    | Mod                   | No              | Mod                                 | Serious             | Bajo                                | 0.37<br>[0.02, 7.4]    | No           | Mod                                                    | Serious           | Bajo          |
| Lu177_ARI   | PARP_AA   | 0.45<br>[0.01, 29.78]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 0.45<br>[0.01, 29.78]  | No           | Mod                                                    | Muy serio         | Bajo          |
| Lu177_ARI   | PARP_ARI  | 1.08<br>[0.05, 21.28]  | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 1.08<br>[0.05, 21.28]  | No           | Mod                                                    | Muy serio         | Bajo          |

| Comparación |          | Evidencia indirecta    |                       |                 |                                     | Evidencia de la red |                                     |                        |              |                                                        |                   |               |
|-------------|----------|------------------------|-----------------------|-----------------|-------------------------------------|---------------------|-------------------------------------|------------------------|--------------|--------------------------------------------------------|-------------------|---------------|
| Brazo 1     | Brazo 2  | HR IC 95%              | Calificación Más Baja | Intransitividad | Comparación indirecta sin impresión | Impresión           | Comparación indirecta sin impresión | HR IC 95%              | Incoherencia | Calificación más alta de evidencia directa o indirecta | Impresión del MAR | Puntaje final |
| Lu177_ARI   | Placebo  | 0.13<br>[0.01, 2.51]   | Mod                   | No              | Mod                                 | Serious             | Bajo                                | 0.13<br>[0.01, 2.51]   | No           | Mod                                                    | Serious           | Bajo          |
| PARP_AA     | PARP_ARI | 2.39<br>[0.04, 154.45] | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 2.39<br>[0.04, 154.45] | No           | Mod                                                    | Muy serio         | Bajo          |
| PARP_AA     | Placebo  | 0.28<br>[0.01, 5.5]    | Mod                   | No              | Mod                                 | Serious             | Bajo                                | 0.28<br>[0.01, 5.5]    | No           | Mod                                                    | Serious           | Bajo          |
| PARP_ARI    | Placebo  | 0.12<br>[0.01, 2.35]   | Mod                   | No              | Mod                                 | Serious             | Bajo                                | 0.12<br>[0.01, 2.35]   | No           | Mod                                                    | Serious           | Bajo          |

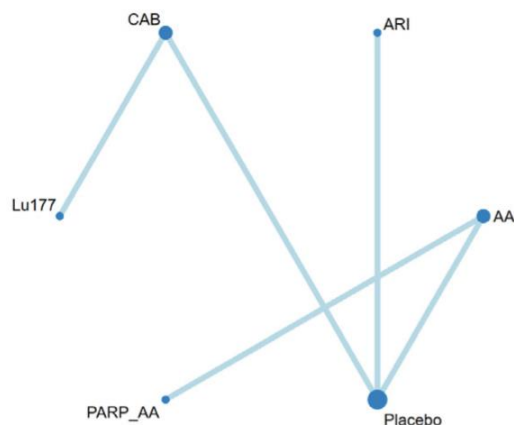
Tomada de Jian et al. (1)



## ✓ Manejo de segunda línea

En segunda línea de manejo, los resultados tampoco fueron significativos. La figura M-3 presenta la red de M-8 describe las comparaciones individuales y la certeza de la evidencia

**Figura M-3. Red de comparaciones indirectas para supervivencia libre de progresión radiológica en segunda línea.**



Tomada de Jiang et al.

Las tecnologías incluidas en este lineamiento que fueron incluidas en este estudio son: inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA), Lutecio-177 (Lu177) y cabazitaxel (CAB).

**Tabla M-7. Tabla de ligas de comparaciones indirectas para supervivencia libre de progresión radiológica en segunda línea.**

| AA                   |                      |                      |                      |                     |         |
|----------------------|----------------------|----------------------|----------------------|---------------------|---------|
| 1.68<br>[0.32, 8.57] | ARI                  |                      |                      |                     |         |
| 0.91<br>[0.18, 4.64] | 0.54<br>[0.1, 2.79]  | CAB                  |                      |                     |         |
| 1.42<br>[0.19, 10.7] | 0.85<br>[0.11, 6.34] | 1.56<br>[0.48, 5.13] | Lu177                |                     |         |
| 1.54<br>[0.47, 5.15] | 0.92<br>[0.12, 6.98] | 1.7<br>[0.22, 13]    | 1.09<br>[0.1, 11.43] | PARP_AA             |         |
| 0.67<br>[0.21, 2.13] | 0.4<br>[0.13, 1.28]  | 0.74<br>[0.23, 2.36] | 0.47<br>[0.09, 2.49] | 0.44<br>[0.08, 2.3] | Placebo |

Para leer la comparación se debe leer la columna más grande (intervención) vs. la más pequeña (referencia). Tomada de Jiang et al. (1)

Las tecnologías incluidas en este lineamiento que fueron incluidas en este estudio son: inhibidores de receptor de andrógenos de segunda generación (ARI), abiraterona acetato (AA), olaparib + abiraterona (PARP\_AA), Lutecio-177 (Lu177) y cabazitaxel (CAB).

**Tabla M-8. Resultados de las comparaciones indirectas y valoración de la certeza de la evidencia para supervivencia libre de progresión radiológica en segunda línea**

| Comparación |         | Evidencia indirecta  |                       |                 |                                     | Evidencia de la red |                                     |                      |              |                                                        |                   |               |
|-------------|---------|----------------------|-----------------------|-----------------|-------------------------------------|---------------------|-------------------------------------|----------------------|--------------|--------------------------------------------------------|-------------------|---------------|
| Brazo 1     | Brazo 2 | HR IC 95%            | Calificación Más Baja | Intransitividad | Comparación indirecta sin impresión | Impresión           | Comparación indirecta sin impresión | HR IC 95%            | Incoherencia | Calificación más alta de evidencia directa o indirecta | Impresión del MAR | Puntaje final |
| AA          | ARI     | 1.68<br>[0.32, 8.57] | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 1.68<br>[0.32, 8.57] | No           | Mod                                                    | Serio             | Bajo          |
| AA          | CAB     | 0.91<br>[0.18, 4.64] | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 0.91<br>[0.18, 4.64] | No           | Mod                                                    | Serio             | Bajo          |
| AA          | Lu177   | 1.42<br>[0.19, 10.7] | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 1.42<br>[0.19, 10.7] | No           | Mod                                                    | Muy serio         | Muy bajo      |
| AA          | PARP_AA | NR                   | NR                    | NR              | NR                                  | NR                  | NR                                  | 1.54<br>[0.47, 5.15] | No           | Mod                                                    | Serio             | Bajo          |
| AA          | Placebo | NR                   | NR                    | NR              | NR                                  | NR                  | NR                                  | 0.67<br>[0.21, 2.13] | No           | Mod                                                    | Serio             | Bajo          |
| ARI         | CAB     | 0.54<br>[0.1, 2.79]  | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 0.54<br>[0.1, 2.79]  | No           | Mod                                                    | Serio             | Bajo          |
| ARI         | Lu177   | 0.85<br>[0.11, 6.34] | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 0.85<br>[0.11, 6.34] | No           | Mod                                                    | Serio             | Bajo          |
| ARI         | PARP_AA | 0.92<br>[0.12, 6.98] | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 0.92<br>[0.12, 6.98] | No           | Mod                                                    | Serio             | Bajo          |
| ARI         | Placebo | NR                   | NR                    | NR              | NR                                  | NR                  | NR                                  | 0.4<br>[0.13, 1.28]  | No           | Mod                                                    | Serio             | Bajo          |
| CAB         | Lu177   | NR                   | NR                    | NR              | NR                                  | NR                  | NR                                  | 1.56<br>[0.48, 5.13] | No           | Mod                                                    | Serio             | Bajo          |
| CAB         | PARP_AA | 1.7<br>[0.22, 13]    | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 1.7<br>[0.22, 13]    | No           | Mod                                                    | Serio             | Bajo          |
| CAB         | Placebo | NR                   | NR                    | NR              | NR                                  | NR                  | NR                                  | 0.74<br>[0.23, 2.36] | No           | Mod                                                    | Serio             | Bajo          |
| Lu177       | PARP_AA | 1.09<br>[0.1, 11.43] | Mod                   | No              | Mod                                 | Muy serio           | Muy bajo                            | 1.09<br>[0.1, 11.43] | No           | Mod                                                    | Muy serio         | Muy bajo      |
| Lu177       | Placebo | 0.47<br>[0.09, 2.49] | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 0.47<br>[0.09, 2.49] | No           | Mod                                                    | Serio             | Bajo          |

| Comparación |         | Evidencia indirecta |                       |                 |                                     | Evidencia de la red |                                     |                     |              |                                                        |                   |               |
|-------------|---------|---------------------|-----------------------|-----------------|-------------------------------------|---------------------|-------------------------------------|---------------------|--------------|--------------------------------------------------------|-------------------|---------------|
| Brazo 1     | Brazo 2 | HR IC 95%           | Calificación Más Baja | Intransitividad | Comparación indirecta sin impresión | Impresión           | Comparación indirecta sin impresión | HR IC 95%           | Incoherencia | Calificación más alta de evidencia directa o indirecta | Impresión del MAR | Puntaje final |
| PARP_AA     | Placebo | 0.44<br>[0.08, 2.3] | Mod                   | No              | Mod                                 | Serio               | Bajo                                | 0.44<br>[0.08, 2.3] | No           | Mod                                                    | Serio             | Bajo          |

Tomada de Jian et al. (1)

- **Olaparib en pacientes con mutación HRR como segunda línea**

La revisión de Zhu et al. (2) evaluó diferentes inhibidores de Poly (ADP-Ribosa) polimerasa en el manejo de pacientes con diagnóstico de CP metastásico resistente a castración con mutaciones HRR en manejo de segunda línea. Realizaron una búsqueda en 2023 y seleccionaron 4 estudios, de los cuales dos estudios evaluaron el efecto de olaparib o de olaparib + abiraterona acetato y evaluaron diferentes desenlaces.

En el caso de supervivencia libre de progresión radiológica, este estudio encontró un HR de 0,49 (ICr95%: 0,38-0,63) con olaparib y de 0,74 (ICr95%: 0,26-2,11) con olaparib + abiraterona comparadas ambas con antiandrógenos solo. Los autores realizaron evaluación por subgrupos comparando olaparib contra antiandrógenos solos, encontrando un HR de 0,15 (ICr95%: 0,10-0,22) en el grupo de BRCA 1/2, de 0,21 (ICr95%: 0,06-0,69) en el grupo de BRCA-2 y de 1,04 (ICr95%: 0,60-1,81) en el grupo de mutación de ATM.

- **Uso de radiofármacos:**

- **Efectividad**

La efectividad de Radio 223 fue evaluada en el ensayo clínico de Parker et al. (ALSYMPCA) (3) en esta CP metastásico resistente a castración que recibieron docetaxel sin mejoría o no pudieron recibirlo. En este estudio encontraron una supervivencia global con un HR de 0,70 (IC95%: 0,58-0,83) comparado con placebo, tiempo al primer evento esquelético con un HR de 0,66 (IC95%: 0,52-0,83).

Para el caso de lutecio-177-PSMA-617, los autores del estudio VISION (4) encontraron en población con CP metastásico resistente a castración PSMA-positivos, una supervivencia global con un HR 0,62 (IC95%: 0,52-0,74), un tiempo al primer evento esquelético con un HR de 0,50 (IC95: 0,40-0,62) y una supervivencia libre de progresión basada en imagen con un HR de 0,40 (IC99,2%: 0,29-0,57).

Los otros desenlaces no fueron evaluados en los estudios incluidos.

## **Resultados de seguridad**

Los autores evaluaron el riesgo de eventos adversos con las diferentes tecnologías. La tabla M-9 describe el riesgo de eventos adversos con cada tecnología.

**Tabla M-9. Riesgo de eventos adversos con las diferentes tecnologías evaluadas.**

|                        | AA                   | ARI                  | CAB                   | DOC                  | DOC + AA              | DOC + ARI              | FARI                  | Lu-177               | Lu-177 + AA           | PARP = AA            | PARP = ARI           | Sip-T                 |
|------------------------|----------------------|----------------------|-----------------------|----------------------|-----------------------|------------------------|-----------------------|----------------------|-----------------------|----------------------|----------------------|-----------------------|
| <b>Fatiga</b>          | 1.1<br>[0.84, 1.69]  | 1.27<br>[0.88, 1.82] | 1.49<br>[0.96, 2.31]  | 1.61<br>[1.15, 2.33] | 1.72<br>[0.9, 3.38]   | 2.59<br>[1.44, 5.12]   | 0.67<br>[0.32, 1.17]  | 1.64<br>[1.08, 2.61] | 3.86<br>[0.72, 2.59]  | 1.63<br>[1.09, 3.06] | 1.66<br>[0.76, 2.75] | 1.1<br>[0.75, 1.72]   |
| <b>Nausea</b>          | 0.98<br>[0.41, 2.32] | 1.13<br>[0.33, 5.39] | 1.58<br>[0.59, 4.32]  | 1.91<br>[0.97, 5.92] | 2.1<br>[0.45, 10.2]   | 2.36<br>[0.69, 9.9]    | 1.39<br>[0.24, 8.13]  | 2.03<br>[0.74, 5.59] | 1.99<br>[0.35, 11.59] | 2.86<br>[0.94, 9.39] | 1.87<br>[0.33, 10.3] | 1.29<br>[0.49, 3.38]  |
| <b>Diarrea</b>         | 1.26<br>[0.63, 2.53] | 1.19<br>[0.6, 2.38]  | 6.27<br>[2.99, 16.13] | 4.06<br>[2.1, 14.94] | 4.65<br>[1.34, 23.71] | 3.36<br>[1.25, 16.8]   | -                     | 3.24<br>[1.51, 8.37] | -                     | 2.29<br>[0.87, 6.06] | 1.24<br>[0.36, 4.16] | 0.86<br>[0.33, 1.95]  |
| <b>Anemia</b>          | 0.84<br>[0.32, 2.1]  | -                    | 1.3<br>[0.5, 3.71]    | 1.36<br>[0.68, 2.82] | 2.35<br>[0.48, 14.83] | 3.67<br>[0.43, 191.93] | -                     | 2.11<br>[0.76, 5.78] | -                     | 2.35<br>[0.35, 9.87] | -                    | 1.01<br>[0.36, 2.52]  |
| <b>Artralgias</b>      | 1.2<br>[0.73, 1.93]  | 1.27<br>[0.58, 2.79] | 1.36<br>[0.53, 2.99]  | 1.53<br>[0.63, 5.73] | -                     | -                      | 3.87<br>[1.05, 14.88] | 2.08<br>[0.65, 6.84] | 1.77<br>[0.17, 4.11]  | 0.69<br>[0.13, 3.24] | 1.06<br>[0.37, 2.92] | 0.94<br>[0.3, 2.81]   |
| <b>Dolor lumbar</b>    | 0.93<br>[0.71, 1.19] | 1.22<br>[0.86, 1.73] | 1.39<br>[0.96, ?]     | 1.52<br>[0.85, 2.78] | -                     | 1.4<br>[0.55, 3.52]    | 1.13<br>[0.61, 2.12]  | 1.55<br>[1.09, 2.27] | -                     | 0.93<br>[0.61, 1.42] | 1.31<br>[0.88, 2.37] | 0.94<br>[0.66, 1.33]  |
| <b>Hipertensión</b>    | 1.17<br>[0.55, 2.41] | 3.25<br>[1.18, 8.93] | -                     | 1.94<br>[0.58, 4.51] | -                     | -                      | 1.67<br>[0.37, 7.45]  | -                    | -                     | 0.87<br>[0.28, 2.43] | 2.91<br>[1.69, 12.3] | 2.69<br>[0.77, 10.80] |
| <b>Dolor de cabeza</b> | -                    | 1.73<br>[0.84, 3.74] | -                     | -                    | -                     | -                      | -                     | -                    | -                     | -                    | 3.88<br>[1.82, 14.2] | 2.37<br>[1.08, 6.39]  |

Tomada y adaptada de Jiang et al. (1)

## • Seguridad

La revisión sistemática de Ventura et al. (5) evaluó la seguridad de estos radiofármacos en estudios de cohortes. Para ello, realizó una búsqueda sistemática e incluyó 65 estudios para Lu-177, Radio-223 y AC-223. La tabla M-10 y M-11 resume los resultados de diferentes eventos adversos relacionados con estas terapias.

**Tabla M-10. Proporción de participantes con eventos adversos de interés y gravedad de ellos que recibieron Lu-177-PSMA.**

| Evento adverso         | Evento grado CTCAE 1/2  |          |                    |         |                             | Evento grado CTCAE 3/5  |          |                    |         |                             |
|------------------------|-------------------------|----------|--------------------|---------|-----------------------------|-------------------------|----------|--------------------|---------|-----------------------------|
|                        | Proporción estimada (%) | IC95%    | I <sup>2</sup> (%) | Valor-p | Intervalo de predicción 95% | Proporción estimada (%) | IC95%    | I <sup>2</sup> (%) | Valor-p | Intervalo de predicción 95% |
| <b>Anemia</b>          | 15.400                  | 5.5–36.1 | 90.400             | <0.001  | 0.5–86.1                    | 11.900                  | 6–22.2   | 78.700             | <0.001  | 1.6–53.1                    |
| <b>Leucopenia</b>      | 16.500                  | 9.1–29.2 | 55.300             | 0.048   | 3.1–54.8                    | 5.400                   | 2–13.4   | 80.000             | <0.001  | 0.4–46.9                    |
| <b>Neutropenia</b>     | 6.000                   | 1.9–17   | 0.000              | 1.000   | 0–99.2                      | 0.000                   | 0.000    | 0.000              | 1.000   | 0.000                       |
| <b>Trombocitopenia</b> | 12.800                  | 6.4–24.5 | 58.000             | 0.026   | 1.7–55.8                    | 5.700                   | 2.7–11.5 | 65.400             | 0.008   | 0.8–31.4                    |

| Evento adverso        | Evento grado CTCAE 1/2  |           |                    |         |                             | Evento grado CTCAE 3/5  |          |                    |         |                             |
|-----------------------|-------------------------|-----------|--------------------|---------|-----------------------------|-------------------------|----------|--------------------|---------|-----------------------------|
|                       | Proporción estimada (%) | IC95%     | I <sup>2</sup> (%) | Valor-p | Intervalo de predicción 95% | Proporción estimada (%) | IC95%    | I <sup>2</sup> (%) | Valor-p | Intervalo de predicción 95% |
| <b>Nefrotoxicidad</b> | 9.400                   | 3.9–20.9  | 88.500             | <0.001  | 0.7–60.6                    | 2.800                   | 1–5.3    | 29.500             | 0.225   | 0–12.2                      |
| <b>Fatiga</b>         | 3.400                   | 1.7–4.5   | 59.800             | 0.058   | 0–37.8                      | 0.000                   | 0.000    | 0.000              | 1.000   | 0.000                       |
| <b>Anorexia</b>       | 8.700                   | 0.3–77.6  | 0.000              | 1.000   | 0–100                       | 0.000                   | 0.000    | 0.000              | 1.000   | –                           |
| <b>Nausea</b>         | 22.800                  | 16.5–30.6 | 0.000              | 0.651   | 13.3–36.1                   | 0.000                   | 0.000    | 0.000              | 1.000   | –                           |
| <b>Vomito</b>         | 6.000                   | 2.5–13.5  | 0.000              | 0.641   | 0–95.7                      | 0.000                   | 0.000    | 0.000              | 1.000   | –                           |
| <b>Estreñimiento</b>  | 25.000                  | 16.9–35.3 | 0.000              | 0.578   | 1.3–89.1                    | 0.000                   | 0.000    | 0.000              | 1.000   | –                           |
| <b>Xerostomia</b>     | 83.700                  | 61.4–94.3 | 73.400             | 0.002   | 12.7–99.4                   | 1.300                   | 0.1–11.8 | 0.000              | 1.000   | 0–55.5                      |

Tomada y adaptada de Ventura et al. (5)

**Tabla M-11. Proporción de participantes con eventos adversos de interés y gravedad de ellos en participantes que recibieron Ra-223.**

| Evento adverso         | Evento grado CTCAE 1/2  |           |                    |         |                             | Evento grado CTCAE 3/5  |          |                    |         |                             |
|------------------------|-------------------------|-----------|--------------------|---------|-----------------------------|-------------------------|----------|--------------------|---------|-----------------------------|
|                        | Proporción estimada (%) | IC95%     | I <sup>2</sup> (%) | Valor-p | Intervalo de predicción 95% | Proporción estimada (%) | IC95%    | I <sup>2</sup> (%) | Valor-p | Intervalo de predicción 95% |
| <b>Anemia</b>          | 18.200                  | 12–26.6   | 96.100             | <0.001  | 2.4–66.5                    | 8.300                   | 6.1–11.2 | 75.800             | <0.001  | 2.3–25.7                    |
| <b>Leucopenia</b>      | 6.900                   | 2.3–18.5  | 96.500             | <0.001  | 0.4–78.8                    | 0.800                   | 0.4–1.7  | 49.300             | 0.549   | 0.1–4.7                     |
| <b>Neutropenia</b>     | 3.700                   | 1.4–9.1   | 96.100             | <0.001  | 0–96.1                      | 1.000                   | 0.3–5.2  | 52.000             | <0.001  | 0–5.4                       |
| <b>Linfopenia</b>      | 3.200                   | 0.5–18.5  | 93.000             | <0.001  | 0–96.7                      | 1.900                   | 0.2–15.5 | 91.500             | <0.001  | 0–98.1                      |
| <b>Trombocitopenia</b> | 6.500                   | 4.2–10.1  | 90.900             | <0.001  | 1–33.6                      | 2.400                   | 1.7–3.3  | 41.000             | 0.033   | 0.9–6                       |
| <b>Nefrotoxicidad</b>  | 6.200                   | 2.6–14    | 0.000              | 0.981   | 0–95.9                      | 0.000                   | 0.000    | 0.000              | 0.999   | 0.000                       |
| <b>Fatiga</b>          | 19.800                  | 12.3–30.1 | 98.000             | <0.001  | 2.7–68.8                    | 1.600                   | 0.9–2.8  | 61.300             | 0.003   | 0.3–8.2                     |
| <b>Diarrea</b>         | 11.700                  | 9–15      | 60.300             | 0.001   | 7.9–17.9                    | 0.700                   | 0.2–2.1  | 53.600             | 0.533   | 0–3.7                       |
| <b>Nausea</b>          | 13.600                  | 9.6–19.1  | 90.800             | <0.001  | 3.2–43.1                    | 0.400                   | 0.2–0.9  | 66.000             | 0.379   | 0.1–1.2                     |
| <b>Vomito</b>          | 7.500                   | 5–10.9    | 89.500             | <0.001  | 2.1–23.3                    | 0.500                   | 0.2–1.2  | 12.800             | 0.328   | 0–1.3                       |
| <b>Estreñimiento</b>   | 6.100                   | 3.2–11.1  | 85.200             | <0.001  | 0.8–35.2                    | 0.600                   | 0.2–1.1  | 0.000              | 0.999   | 0–0.4                       |
| <b>Anorexia</b>        | 9.800                   | 8.2–11.6  | 0.000              | 0.626   | 7.6–12.5                    | 1.200                   | 0.3–5.7  | 78.700             | <0.001  | 0–36.1                      |
| <b>Astenia</b>         | 3.000                   | 1.8–5     | 80.500             | 0.002   | 0.6–14.2                    | 0.400                   | 0.1–1.2  | 70.800             | 0.016   | 0–9.6                       |

Tomada y adaptada de Ventura et al. (5)

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## Anexo M.2 Resultados previos evaluación económica pregunta 4

Para el grupo poblacional 4, cáncer de próstata metastásico resistente a castración en primera y segunda línea no se pueden realizar comparaciones directas entre las tecnologías de evaluación debido a que las indicaciones de cada estrategia terapéutica son distintas. Sin embargo, se realizó el ejercicio de comparación con la evidencia clínica encontrada. Se obtuvieron cinco comparaciones directas, además de la presentada en el informe del Posicionamiento.

En la tabla M-6, se presentan los resultados de costo-utilidad para la comparación de mitoxantrona versus cabazitaxel. El mayor costo de cabazitaxel no compensa la ganancia en utilidad, teniendo una RICE de más de mil millones de pesos. Por lo tanto, la alternativa costo-efectiva en este caso es mitoxantrona.

La tabla M-7 se muestran los resultados de la comparación entre abiraterona, enzalutamida y olaparib. En relación, con abiraterona que es la alternativa más económica, enzalutamida es una alternativa dominada pues es más costosa y no presenta más AVAC y olaparib no es costo-efectivo dado que presenta una RICE de más de 20 mil millones de pesos. Por ende, el ordenamiento según el BMN muestra a abiraterona en la primera posición.

Los resultados de costo efectividad de comparar enzalutamida con placebo se observan en la tabla M-8. Se evidencia que la RICE de agregar enzalutamida está cerca de los 2 mil millones de pesos, por lo cual no es costo-efectiva y en el ordenamiento de BMN se considera no agregar medicamento (placebo) como la mejor alternativa.

En la tabla M-9, similar al caso anterior se muestran los resultados de agregar abiraterona. La RICE para esta alternativa es de aproximadamente 2 mil millones de pesos, un valor considerablemente lejano a la disposición a pagar en Colombia. Luego, en esta comparación la mejor alternativa en términos de BMN es no agregar nada (placebo).

Por último, la tabla M-10 presenta los resultados costo-utilidad de abiraterona, enzalutamida y cabazitaxel. Abiraterona es la alternativa más económica, con



relación a esta enzalutamida es dominada ya que presenta costos mayores sin ganancia en utilidad. Por su parte, cabazitaxel tiene una RICE alrededor de 600 millones de pesos superando la disposición a pagar por un AVAC y por ende, no es una alternativa costo-efectiva. En ese sentido, abiraterona queda como la primera alternativa en esta comparación.

**Tabla M-12. Resultados caso base grupo poblacional 4 – TROPIC**

| TPA | Medicamento  | Costo total    | AVAC | Δ Costos      | Δ AVAC | RICE             | BMN            | Orden (1 UCE) |
|-----|--------------|----------------|------|---------------|--------|------------------|----------------|---------------|
| TPA | Mitoxantrona | \$ 52.164.934  | 0,35 |               |        |                  | -\$ 42.417.685 | 1             |
| TPA | Cabazitaxel  | \$ 107.629.571 | 0,4  | \$ 55.464.637 | 0,1    | \$ 1.109.292.730 | -\$ 96.489.857 | 2             |

Fuente: Elaboración propia

**Tabla M-13. Resultados caso base grupo poblacional 4 – PROfound**

| TPA | Medicamento  | Costo total    | AVAC | Δ Costos       | Δ AVAC | RICE              | BMN             | Orden (1 UCE) |
|-----|--------------|----------------|------|----------------|--------|-------------------|-----------------|---------------|
| TPA | Abiraterona  | \$ 82.615.387  | 0,43 |                |        |                   | -\$ 70.640.194  | 1             |
| TPA | Enzalutamida | \$ 100.945.272 | 0,43 | \$ 18.329.885  | 0,0    | Dominada          | -\$ 88.970.079  | 2             |
| TPA | Olaparib     | \$ 283.663.160 | 0,44 | \$ 201.047.773 | 0,0    | \$ 20.104.777.334 | -\$ 271.409.475 | 3             |

Fuente: Elaboración propia

**Tabla M-14. Resultados caso base grupo poblacional 4 – PREVAIL**

| TPA | Medicamento  | Costo total    | AVAC | Δ Costos       | Δ AVAC | RICE             | BMN             | Orden (1 UCE) |
|-----|--------------|----------------|------|----------------|--------|------------------|-----------------|---------------|
| TPA | Placebo      | \$ 89.624.290  | 0,62 |                |        |                  | -\$ 72.357.733  | 1             |
| TPA | Enzalutamida | \$ 221.407.781 | 0,68 | \$ 131.783.491 | 0,1    | \$ 2.196.391.518 | -\$ 202.470.267 | 2             |

Fuente: Elaboración propia

**Tabla M-15. Resultados caso base grupo poblacional 4 – COU-AA-302**

| TPA | Medicamento | Costo total    | AVAC | Δ Costos      | Δ AVAC | RICE             | BMN             | Orden (1 UCE) |
|-----|-------------|----------------|------|---------------|--------|------------------|-----------------|---------------|
| TPA | Placebo     | \$ 83.923.613  | 0,64 |               |        |                  | -\$ 66.100.071  | 1             |
| TPA | Abiraterona | \$ 147.787.424 | 0,67 | \$ 63.863.811 | 0,0    | \$ 2.128.793.688 | -\$ 129.128.403 | 2             |

Fuente: Elaboración propia

**Tabla M-16. Resultados caso base grupo poblacional 4 – CARD**

| TPA | Medicamento  | Costo total    | AVAC | Δ Costos      | Δ AVAC | RICE           | BMN             | Orden (1 UCE) |
|-----|--------------|----------------|------|---------------|--------|----------------|-----------------|---------------|
| TPA | Abiraterona  | \$ 66.829.972  | 0,3  |               |        |                | -\$ 58.475.187  | 1             |
| TPA | Enzalutamida | \$ 90.035.490  | 0,3  | \$ 23.205.517 | 0,0    | Dominada       | -\$ 81.680.704  | 2             |
| TPA | Cabazitaxel  | \$ 141.203.884 | 0,42 | \$ 74.373.912 | 0,1    | \$ 619.782.601 | -\$ 129.507.185 | 3             |

Fuente: Elaboración propia

## Análisis de sensibilidad

El análisis de sensibilidad determinístico muestra que los resultados anteriores son robustos ante cambios de las tasas de descuento del 0%, 3%, 5% y 9%. Esto se mantiene para todas comparaciones del grupo poblacional 4 (Ver panel A de la Figura M-4 a la figura M-8)

Los resultados para el estudio TROPIC se presentan en la Figura M-4, donde se observa que las utilidades de progresión de la enfermedad es una variable clave del BMN tanto para mitoxantrona como cabazitaxel. Así mismo, para cabazitaxel la variable que afecta mayormente el BMN es el costo del tratamiento.

La Figura M-5 **Error! No se encuentra el origen de la referencia.**, muestra el análisis para la comparación del estudio PROfound. El BMN, para abiraterona y enzalutamida, se ve afectado principalmente por la utilidad de progresión de la enfermedad. Mientras que para olaparib la variable de mayor impacto en el BMN es el costo del tratamiento seguido de la ponderación de utilidad del estado libre de progresión.

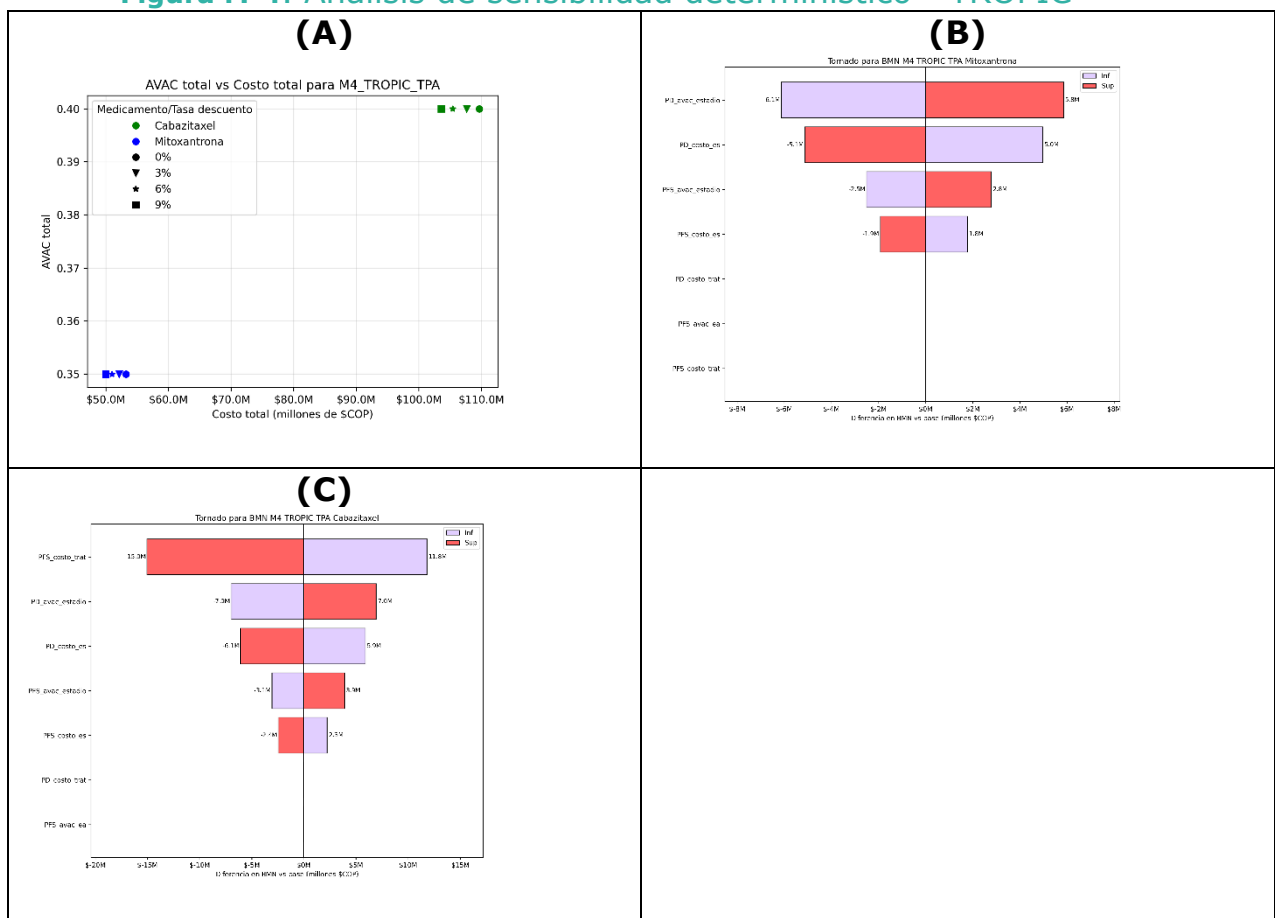
Por su parte, en la comparación del estudio PREVAIL la Figura M-6, muestra que el BMN de enzalutamida se ve afectado principalmente por el costo del tratamiento y la ponderación de utilidad del estado de salud libre de progresión.

Así mismo, la Figura M-7 muestra el diagrama de tornado basado en el estudio COU-AA-302. Las variables que afectan en mayor medida el BMN para

abiraterona, al igual que el caso anterior, son el costo del tratamiento y la ponderación de utilidad del estado de salud libre de progresión.

Finalmente, en la Figura M-8 se observa que el costo del tratamiento es la variable que afecta en mayor medida el cálculo del BMN para todas las alternativas de comparación del estudio CARD, es decir, abiraterona, cabazitaxel, enzalutamida. Luego, le siguen las ponderaciones de utilidad de estado libre de progresión.

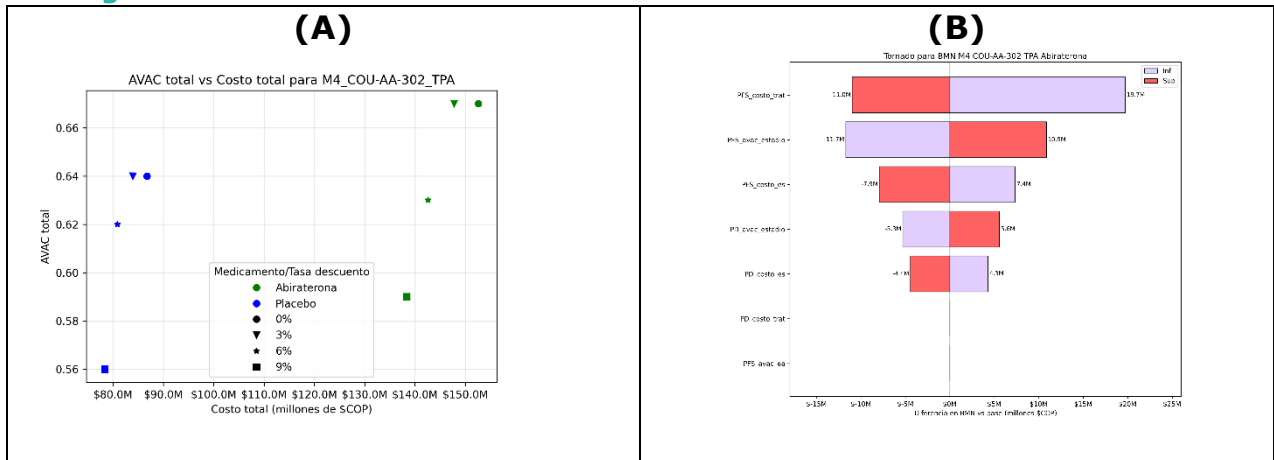
**Figura M-4. Análisis de sensibilidad determinístico - TROPIC**



Fuente: Elaboración propia

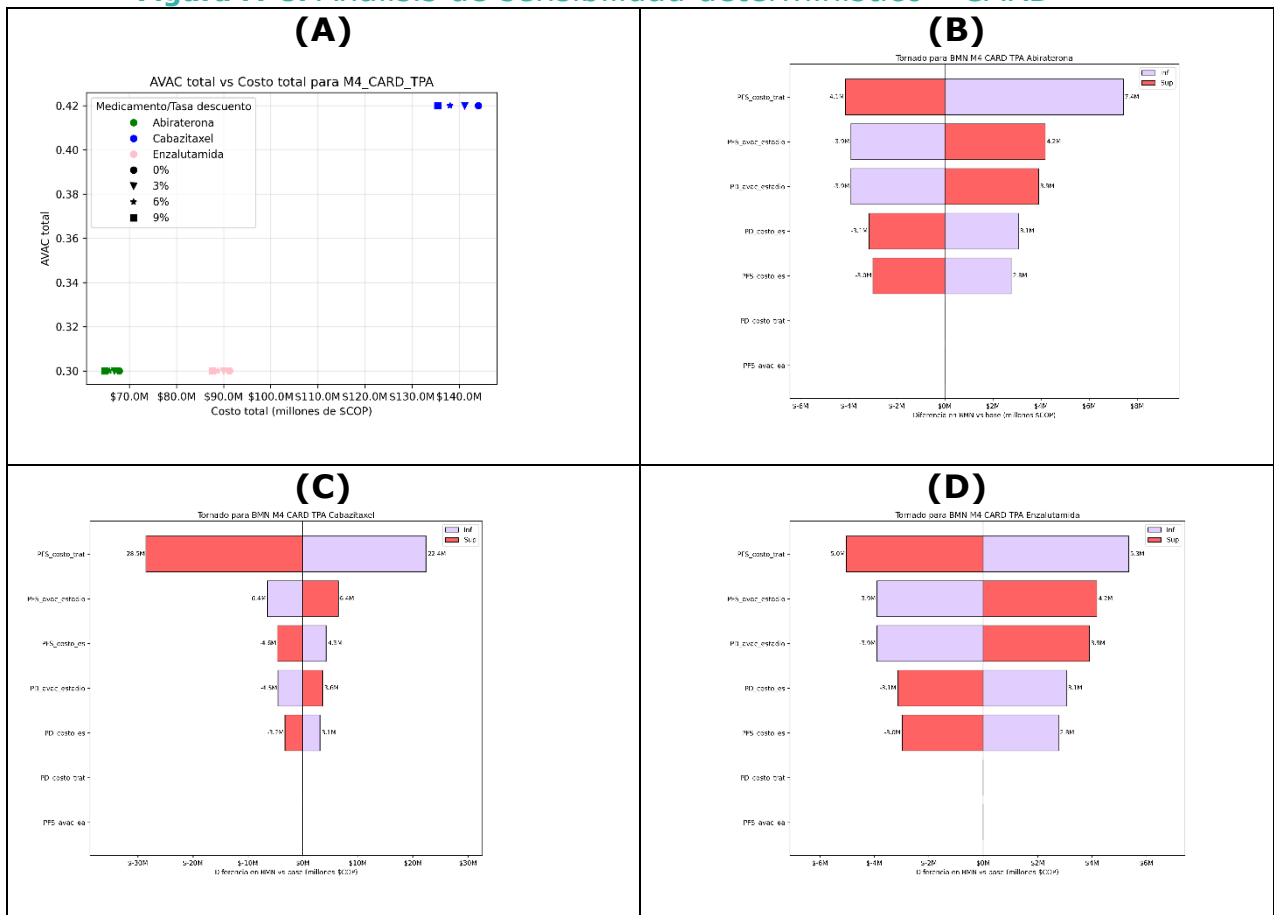


**Figura M-7. Análisis de sensibilidad determinístico – COU-AA-302**



Fuente: Elaboración propia

**Figura M-8. Análisis de sensibilidad determinístico - CARD**



## Anexo N. Metodología de cálculo de precios de medicamentos y procedimientos

A continuación, se presenta la metodología usada para la estimación de costos unitarios y costo del tratamiento total de las tecnologías que se evaluarán en el Posicionamiento terapéutico para el tratamiento del cáncer de próstata. En este estudio se considerará la perspectiva de Sistema General de Seguridad Social en Salud (SGSSS), es decir, se tienen en cuenta los costos directos en salud con cargo a recursos públicos.

Con el fin de determinar el costo del tratamiento por grupo de análisis, se llevó a cabo el proceso de identificación, medición y valoración de los recursos relacionados. Para esto, se inició con una revisión de la información INVIMA a corte de mayo del 2025 (1). Esta revisión se realizó a partir del Código Único de Medicamentos (CUM) y el Identificador Único de Medicamentos (IUM) para los medicamentos. De igual manera, el proceso de identificación estuvo acompañado por la revisión de guías, artículos de referencia y consulta a los expertos clínicos en los espacios de mesas de trabajo.

Para el cálculo de los costos unitarios de los medicamentos se usó la base de datos del SISMED (Sistema de Información de Precios de Medicamentos) de enero a diciembre 2024 (2), la base de datos del INVIMA a mayo del 2025 (1) y la base de datos de la CNPMDM (Comisión Nacional de Precios de Medicamentos y Dispositivos Médicos) referente al listado por unidad de regulación para cada mercado relevante con corte a mayo del 2025 (3); esta última con el fin de identificar los precios máximos regulados de las tecnologías del análisis. A continuación, se presenta, la metodología de cálculo de los precios unitarios de los medicamentos

### 1.1. Costos unitarios de medicamentos

Teniendo en cuenta la perspectiva de la evaluación económica, la estimación de precios se realiza considerando el canal institucional, en el cual se realizan las compras y ventas de medicamentos que se dispensan a la población con cargo a recursos públicos. La consulta y estimación de los costos unitarios de medicamentos, se desarrolló en tres etapas: búsqueda y filtración a partir del SISMED, parametrización del producto farmacéutico y cálculo del costo unitario por Unidad Mínima de Concentración (UMC).

## Etapa 1: Búsqueda, extracción, filtrado y análisis de valores atípicos de los reportes de precios a partir del SISMED

En la búsqueda, se identificaron los expedientes, los Códigos Únicos de Medicamentos (CUM) y los Identificadores Únicos de Medicamentos (IUM), correspondientes a cada uno de los principios activos (PA) involucrados en el estudio. La extracción de la información se realizó por medio de la base de datos del INVIMA a partir de los registros vigentes y en trámite de renovación con corte a mayo de 2025 (1). Con los códigos CUM e IUM obtenidos, se buscó en la base de datos del SISMED de enero a diciembre de 2024 (2). El proceso de consulta de los registros tuvo en cuenta los siguientes filtros:

- Rol actor reportante: “elabora o importa”.
- Transacción SISMED: “transacción primaria institucional”.
- Tipo reporte precio: “venta”.

Con los registros de SISMED, se realizó un filtrado por consistencia de los datos y un análisis de valores atípicos que parte del supuesto de que los precios de medicamentos para un mismo CUM o IUM, una misma unidad de medida y en un período corto (un año) no deberían presentar cambios sustanciales.

Adicionalmente, se revisaron las circulares de regulación de precios de la CNPMDM a mayo de 2024, puesto que es la última fecha de emisión de normas en esta materia por parte del ente competente, con el fin de identificar los precios máximos regulados de todas las tecnologías del análisis.

## Etapa 2: Parametrización y ajuste de la información del producto farmacéutico y de las variables de los reportes de precios

La etapa de parametrización tiene el propósito de asegurar que los datos de los registros sean comparables entre sí, es decir, que cada variable presente un parámetro homogenizado para su análisis. Se construyeron las variables Principio Activo (PA), clasificación de la forma farmacéutica/vía de administración (FF/VA), presentación comercial (unidad de medida y cantidad), unidades farmacéuticas (unidad de medida y cantidad), concentración (unidad de medida y cantidad) y la cantidad total del principio activo como el producto de las cantidades de las variables anteriores (unidad de medida y cantidad).

### Etapa 3: Cálculo del costo unitario por unidad mínima de concentración (UMC) y búsqueda de los precios regulados o valores de referencia

La estimación de los precios de los medicamentos tiene dos componentes. El primero consiste en determinar las UMC de la cantidad total de los PA vendidos. La cantidad total de PA vendido se calculó como el producto de las unidades vendidas y la cantidad total del principio activo y con ello se calculó la participación de mercado de cada registro de acuerdo con cada CUM. Con estas variables, se determinaron los precios por UMC (el precio verificado sobre la cantidad total de principio activo) y los precios ponderados (precios por UMC por la participación de mercado) para el inferior, el medio y el superior. Estos precios ponderados se contrastaron con el precio regulado de la CNPMDM por principio activo (4).

#### 1.2. Costos unitarios de procedimientos

En el contexto colombiano existen varias fuentes de información que permiten calcular los precios de los procedimientos. La consulta y estimación de los costos unitarios de procedimientos, se desarrolló en tres etapas: búsqueda y filtración a partir de las bases de datos de Suficiencia/Recobros/MIPRES, análisis de valores atípicos y cálculo de los precios y búsqueda de precios regulados.

#### Etapa 1: Búsqueda, extracción y filtrado de los reportes de precios a partir de las bases de datos de Suficiencia/Recobros/MIPRES

La elección de las bases de datos de consulta depende primordialmente de la fuente de financiación, pues la financiación puede ser con recursos con cargo a la unidad de pago por capitación (UPC) o vía presupuestos máximos (MIPRES). Se realizó la consulta en la base de datos de Suficiencia de la UPC 2023, donde se recopiló toda la información suministrada por las EAPB a MinSalud, de acuerdo con el estado de inclusión de tecnologías en salud financiadas con cargo a la UPC. No fue necesario hacer búsqueda en la base de datos MIPRES, ya que todos los procedimientos están financiados con recursos con cargo a la UPC.

Antes del proceso de cálculo, se tuvo en cuenta la clasificación de procedimientos simples (se analizan de manera independiente) y complejos (involucra otras prestaciones de salud), así como la forma de pago de cada uno. Para el caso de los procedimientos simples, se extrajeron los reportes para cada año de la base de datos de suficiencia a partir de los CUPS o la descripción de la tecnología de



interés, considerando únicamente la información reportada en la forma de pago por “Evento” (identificados en el campo “Forma de reconocimiento” con la letra S). Para los procedimientos clasificados como complejos, se consideraron las observaciones reportadas en la forma de reconocimiento “Por paquete” (identificados en el campo “Forma de reconocimiento” con la letra P).

## Etapa 2: Análisis de valores atípicos o ajuste de los registros

El propósito de este análisis es calcular los precios con mayor precisión mediante la disminución de la distorsión generada por los valores extremos en la estimación de los precios a utilizar en el análisis económico.

El análisis se construye a partir de una combinación equiprobable entre una aproximación robusta de la variabilidad y un diagrama de caja y bigotes, así los límites para determinar las observaciones a incluir están dados por:

$$\begin{aligned} \text{Límite inferior} &= \frac{1}{2} \times (\min_{\text{aproximación robusta de la variabilidad}} + \min_{\text{diagrama caja-bigotes}}) \text{ y} \\ \text{Límite superior} &= \frac{1}{2} \times (\max_{\text{aproximación robusta de la variabilidad}} + \max_{\text{diagrama caja-bigotes}}) \end{aligned}$$

En donde, el *min* y el *máx* son respectivamente los valores mínimos y máximos de cada aproximación, que se calculan como:

- Aproximación robusta de la variabilidad (tres desviaciones sobre la mediana): los datos anómalos son las observaciones por fuera del intervalo

$$Mdn(x) \pm 3 * d.m.(x)$$

donde  $Mdn(x)$  hace referencia a la mediana y  $d.m.(x)$  a la desviación media absoluta de la mediana.

- Diagrama de caja-bigotes: los datos anómalos son las observaciones por fuera del intervalo

$$Q1 \pm 1,5(Q3 - Q1)$$

Donde  $Q1$  hace referencia al primer cuartil y  $Q3$  al tercer cuartil.

## Etapa 3: Cálculo de los precios

Los precios se deflactaron al año 2024 con la información del IPC, extraída del DANE. Se generaron diferentes estadísticas descriptivas de la malla de datos



depurada. Se utilizó como medida de tendencia central del precio unitario, la mediana de dicha malla de datos, y se tomó el primer y tercer cuartil para construir un intervalo de precios sobre la mediana.



## **Anexo O. Información de Costo detallado de las tecnologías de evaluación y de los eventos en salud**

Se presentan en el archivo suplementario titulado **“Anexo O. Costo detallado de las tecnologías de evaluación y de los eventos en salud”**

