

Plain language summary of the design of the TALAPRO-2 study comparing talazoparib and enzalutamide versus enzalutamide and placebo in men with metastatic castration-resistant prostate cancer

Neeraj Agarwal¹, Arun Azad², Neal D Shore³, Joan Carles⁴, Andre P Fay⁵, Curtis Dunshee⁶, Lawrence Ivan Karsh⁷, Maria Luisa Paccagnella⁸, Nicola Di Santo⁹, Mohamed Elmeligy¹⁰, Xun Lin¹⁰, Akos Czibere¹¹ & Karim Fizazi¹²

¹Huntsman Cancer Institute (NCI-CCC) at the University of Utah, Salt Lake City, UT, USA; ²Peter MacCallum Cancer Centre, Melbourne, Australia; ³Carolina Urologic Research Center, Myrtle Beach, SC, USA; ⁴Vall d'Hebron Institute of Oncology, Vall d'Hebron University Hospital, Barcelona, Spain; ⁵PUCRS School of Medicine Grupo Oncoclínicas, Porto Alegre, Brazil; ⁶Urological Associates of Southern Arizona, Tucson, AZ, USA; ⁷The Urology Center of Colorado, Denver, CO, USA; ⁸Pfizer Inc., Groton, CT, USA; ⁹Pfizer Inc., Durham, NC, USA; ¹⁰Pfizer Inc., La Jolla, CA, USA; ¹¹Pfizer Inc., Cambridge, MA, USA; ¹²Institut Gustave Roussy, University of Paris-Saclay, Villejuif, France

First draft submitted: 14 April 2022; Accepted for publication: 18 July 2022; Published online: 11 August 2022

Summary

What is this summary about?

This summary describes the design of an ongoing research study (also known as a clinical trial) called TALAPRO-2. The TALAPRO-2 trial is testing the combination of two medicines called **talazoparib** and **enzalutamide**

as a first treatment in adult men with metastatic castration-resistant prostate cancer. The study began in December 2017 and has enrolled 1037 adult men with metastatic castration-resistant prostate cancer from 26 countries.

What is metastatic castration-resistant prostate cancer?

Metastatic castration-resistant prostate cancer is a type of cancer that has advanced beyond the prostate and continues to grow even when testosterone levels in the blood are suppressed.

Which medicines are being tested?

The combination of **talazoparib** plus **enzalutamide** will be compared with **enzalutamide** plus **placebo**. **Enzalutamide** is approved to treat men with prostate cancer. **Talazoparib** is not approved to treat men with prostate cancer. A **placebo** does not contain any active ingredients and is also known as a sugar pill.

What are the aims of the TALAPRO-2 trial?

The TALAPRO-2 trial will find out if combining **talazoparib** with **enzalutamide** increases the length of time the men in the study live without their cancer getting worse compared with **enzalutamide** plus **placebo**. The study will also measure how long men in the study live and any side effects the men have while they are taking the study medicines. Researchers are also testing the DNA from the tumor cells of all men in the study to find out if they have faulty DNA repair genes.

Who is this article for?

This summary was written by the authors of the original article to help patients and their caregivers, as well as health professionals, better understand the 2-part design of the TALAPRO-2 study.

Where can I find the original article on which this summary is based?

You can read the original article published in the journal *Future Oncology* for free at: <https://www.futuremedicine.com/doi/10.2217/fo-2021-0811>

How to say (double-click on the icon to play sound)...



Enzalutamide: (EN-zuh-LOO-tuh-mide)

Talazoparib: (tal-a-ZOE-pa-rib)

What is metastatic castration-resistant prostate cancer?



Prostate cancer is one of the most common cancers in men. It forms in the tissues of the prostate, a male reproductive gland found below the bladder.



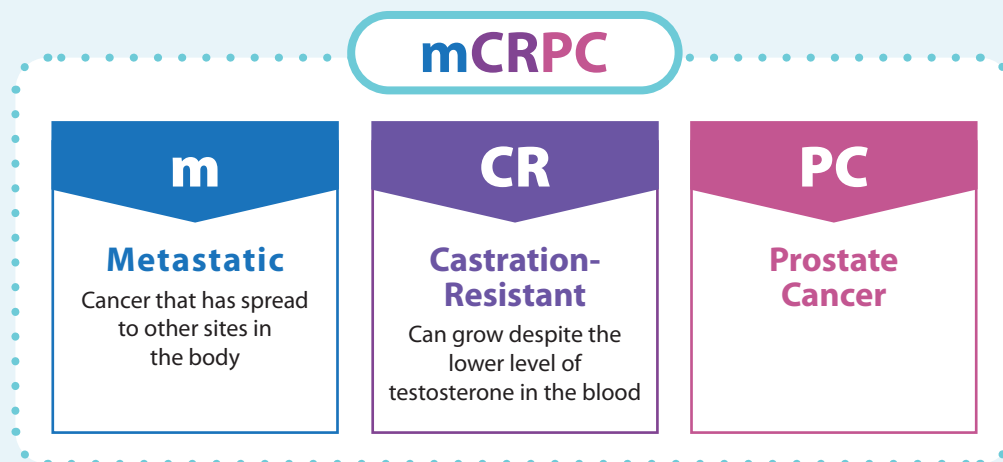
Most prostate cancers need male sex hormones (also called androgens), such as **testosterone**, for them to grow.

- Hormones work by carrying messages from one part of the body to another.



Lowering testosterone levels in the blood is a common treatment for prostate cancer.

- This may be done through surgery to remove the testicles (known as surgical castration) or testosterone suppression therapy (known as chemical castration).
 - Testosterone suppression therapy includes medications that lower the production of testosterone in the testicles.
- Prostate cancer that stops growing or shrinks when treated with medicines that lower testosterone levels in the blood is called **castration-sensitive prostate cancer**.
- In some men, surgical or chemical castration may work at first and later stop working. For other men, it may not work at all. In both cases, this type of cancer is called **castration-resistant prostate cancer**.
 - If the cancer does not respond to treatments that lower testosterone levels in the blood and it has spread beyond the prostate to other sites in the body, it is known as **metastatic castration-resistant prostate cancer** (also called **mCRPC** for short).



What is the role of DNA damage in prostate cancer?



DNA is a molecule that tells cells in the body how and when to make proteins.

- Proteins control how a living thing will look and function.
- Genes are a part of DNA that tells cells in the body how to make proteins. Genes give you your height, natural hair color, and eye color.



Every day, processes inside the cell and events outside the cell (like radiation from the sun) damage DNA. DNA is important, so the cell uses systems made of proteins to find and repair the damage in the DNA.

- If the cell cannot repair the damaged DNA, there is a risk the cell might grow into cancer. In most cases, the cell dies to prevent this. In rare cases, the cell might not die and a tumor may develop.



Some men with prostate cancer have faulty DNA repair genes in their tumors. Faulty DNA repair genes make faulty DNA repair proteins.

- Sometimes faulty DNA repair genes cause cancer because the cell cannot repair DNA very well.
- Faulty DNA repair genes can also make the tumor sensitive to some cancer treatments, including **talazoparib**.

What is talazoparib?



PARP proteins are important for finding damaged DNA. PARP stands for poly(ADP-ribose) polymerase.



Talazoparib is a PARP inhibitor. A PARP inhibitor stops PARP proteins from working.



If **talazoparib** stops PARP proteins from working and the DNA repair proteins are faulty at the same time, the tumor cells cannot grow. This means the tumor cells are more likely to die than cells with normal DNA repair proteins.

What is enzalutamide?



Enzalutamide is approved to treat men with prostate cancer.

Enzalutamide works by stopping androgens (like testosterone) from helping prostate cancer cells to grow.



Enzalutamide may make the tumor cells behave like they have faulty DNA repair systems, even if the cells do not have faulty DNA repair genes.

Why are researchers studying the combination of talazoparib and enzalutamide?



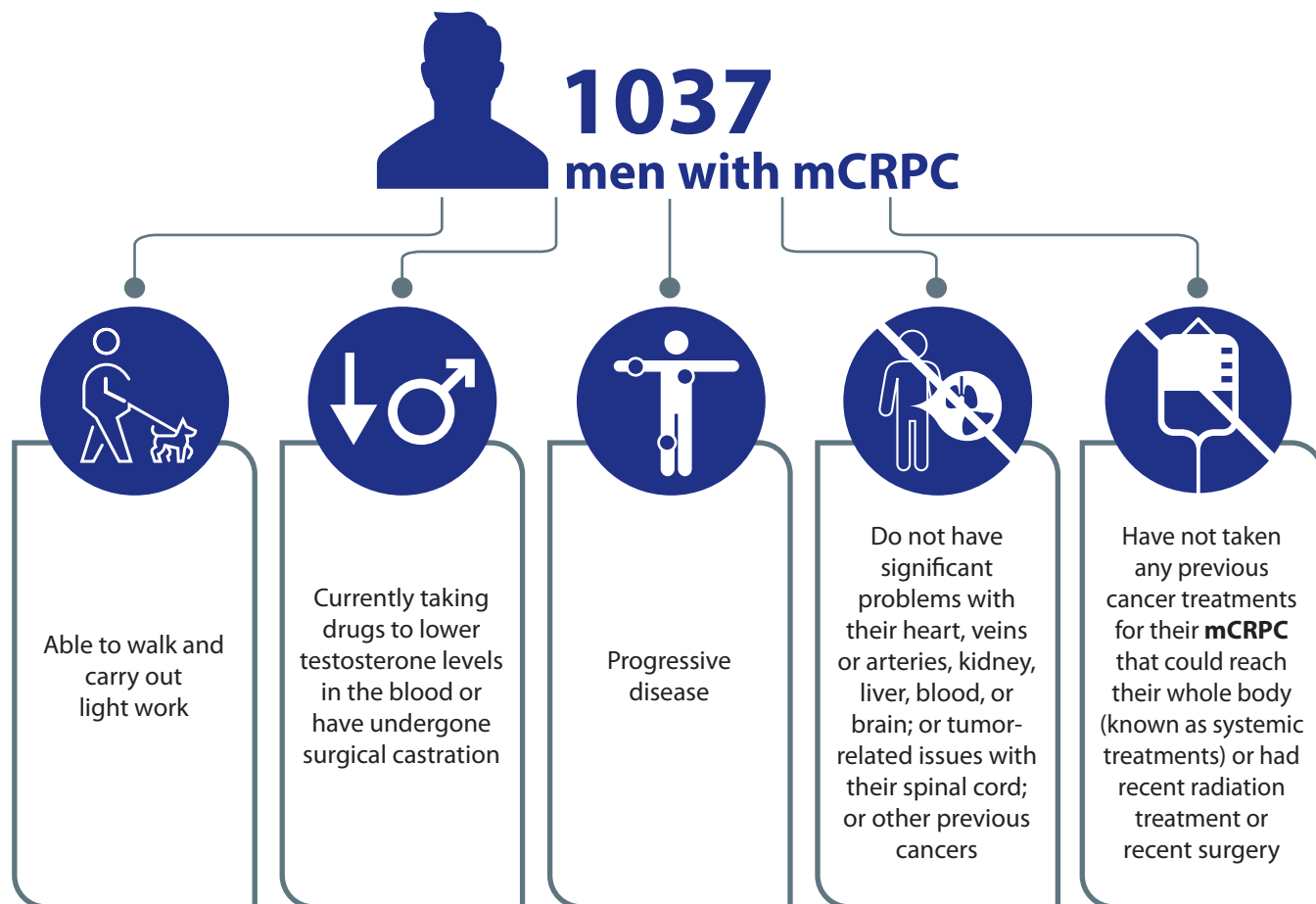
- TALAPRO-2 will find out if combining **talazoparib** with **enzalutamide** will increase the length of time the men in the study live without their cancer getting worse when compared with men receiving **enzalutamide** and **placebo**.
- Earlier studies suggest that **talazoparib** and **enzalutamide** may work well together:
 - **Enzalutamide** may make the cancer cells more sensitive to **talazoparib**.
 - Androgens (like testosterone) also need PARP proteins to help cancer cells grow. Therefore, **talazoparib** may make cancer cells more sensitive to **enzalutamide**.

Who is taking part in the TALAPRO-2 study?

The TALAPRO-2 study is a Phase 3 study.

- A Phase 3 study takes place after the early testing stages to find out if a treatment works in a larger number of patients with a particular disease.

Enrollment for the TALAPRO-2 study took place in two parts. It began in December 2017 and is now complete after enrolling 1037 adult men (19 men in part 1 and 1018 men in part 2). All men have **mCRPC** with mild (or no) symptoms and have the following characteristics:



Progressive disease means the cancer is growing, spreading, or getting worse

Prostate cancer is considered progressive if the man's prostate-specific antigen (also known as PSA) values increase, or if scans show growth or spread of the cancer in the bones or other tissues in the body

PSA is a protein made by the prostate gland and found in the blood. In men who have prostate cancer, levels of PSA are often higher than in men who do not have prostate cancer

Part 1 of the TALAPRO-2 study

- Part 1 of the TALAPRO-2 study is complete and involved 19 men.
- The aim of part 1 was to find out which dose of **talazoparib** should be used safely in combination with **enzalutamide** in part 2 of the study.



Based on the results of part 1, researchers found the appropriate starting dose of **talazoparib** to be **0.5 mg per day**



The dose of **enzalutamide** is **160 mg per day**

Part 2 of the TALAPRO-2 study

- Part 2 enrollment is complete (no additional men will be enrolled). The goal was to enroll 1018 men.
 - Men with and without errors in DNA repair genes are included in the study.

All of the men in part 2 of the study are taking enzalutamide:



Half of the men were randomly assigned to also receive **talazoparib**



The other half of the men are taking a **placebo** instead of **talazoparib**



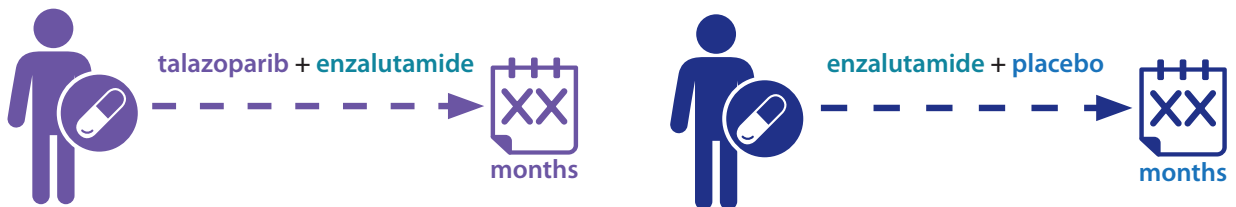
A **placebo** does not contain any active ingredients (it is also known as a sugar pill). The **placebo** and study drugs look alike. Sometimes, people feel their disease has improved just because they are taking a pill, even if it is only a **placebo**. This study is using a **placebo pill** to make sure that any changes to the men's cancer are due to **talazoparib** in combination with **enzalutamide**, and not just because the men are taking an extra pill.

Neither the men in the study nor the health professionals looking after them will know whether the men are taking **talazoparib** or **placebo**.

What are the aims of the TALAPRO-2 study?

- Part 2 of the TALAPRO-2 study will find out if combining **talazoparib** with **enzalutamide**, as a man's first treatment for **mCRPC**, will increase the length of time the men in the study live without their cancer getting worse compared with **enzalutamide** plus **placebo**.
 - Researchers will investigate these treatments in men with and without errors in selected DNA repair genes.

How long men live without their cancer getting worse



- The men will have diagnostic imaging (CT, MRI, and bone scan) every 8 to 12 weeks to measure changes in the size or number of sites with cancer outside of the prostate.
 - The scan results will tell researchers if the cancer is shrinking, growing, or staying the same.
- Researchers will also look at other outcomes such as how long the men in the study live overall and any side effects they may have.
 - A side effect is a reaction (expected or unexpected) to a medicine or treatment you take.



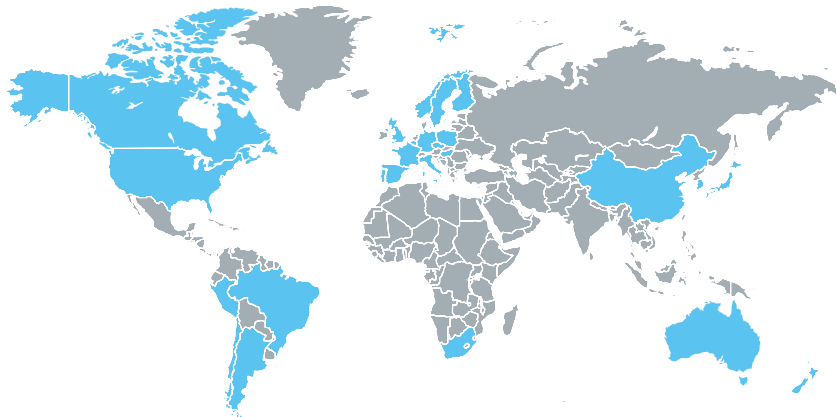
A CT scan uses a computer linked to an x-ray machine to make detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create images of tissues and organs

An MRI uses radio waves and a powerful magnet linked to a computer to make detailed pictures of areas inside the body. These pictures can show the difference between normal tissue and tissue that may be cancer

Where is the study taking place?

TALAPRO-2 is currently studying men in 26 countries

Argentina	Italy
Australia	Japan
Belgium	New Zealand
Brazil	Norway
Canada	Peru
Chile	Poland
China	Portugal
Czech Republic	Republic of Korea
Finland	South Africa
France	Spain
Germany	Sweden
Hungary	United Kingdom
Israel	United States



Who is sponsoring this study?

The TALAPRO-2 trial is sponsored by Pfizer Inc. Astellas Pharma Inc. is providing **enzalutamide**. Pfizer and the authors would like to thank all of the men who participated or are participating in this study and their families, as well as the treating physicians, research nurses, study coordinators, and operations staff.

Where can I find more information?

Original article

The full title of the original article is 'Talazoparib plus enzalutamide in metastatic castration-resistant prostate cancer: TALAPRO-2 phase III study design'. You can read the article for free at: <https://www.futuremedicine.com/doi/full/10.2217/fon-2021-0811>

The full citation of the original article is:

Agarwal N, Azad A, Shore ND *et al.*: Talazoparib plus enzalutamide in metastatic castration-resistant prostate cancer: TALAPRO-2 phase III study design. *Future Oncol.* 18(4) doi.org/10.2217/fon-2021-0811

Trial registration site

You can read more about the Phase 3 TALAPRO-2 study at the following trial registration website:

[Clinicaltrials.gov - trial number NCT03395197](https://clinicaltrials.gov/ct2/show/study/NCT03395197)

For more information on clinical studies in general, please visit:

<https://www.clinicaltrials.gov/ct2/about-studies/learn>

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/what-clinical-trials-are>

Educational resources

You can read more about prostate cancer on the American Society of Clinical Oncology Cancer.Net website at:

<https://www.cancer.net/cancer-types/prostate-cancer>

Patient-focused information on prostate cancer from the NIH is available at:

<https://www.cancer.gov/types/prostate>

Technical abbreviations

CT stands for computed tomography. DNA stands for deoxyribonucleic acid. mCRPC stands for metastatic castration-resistant prostate cancer. MRI stands for magnetic resonance imaging. PARP stands for poly(ADP-ribose) polymerase. PSA stands for prostate-specific antigen.

Financial & competing interests disclosure

Full author disclosure information can be found in the original article.

Writing support for this summary was provided by Emily Messina of CMC AFFINITY, a division of IPG Health Health Medical Communications, and was funded by Pfizer.