Lay Language Summary

ZZ-FIRST

First results from ZZFIRST: a randomized phase II trial of enzalutamide with or without talazoparib in metastatic hormone-naïve prostate cancer

IMPORTANT:

- The document contains the summary of a clinical trial, and its sole purpose is to communicate the results of it to the general public.
- This document is not intended to promote recruitment or provide medical advice.
- The results reflected in this document may contradict those of other trials.
- It is not recommended to make decisions based on the information collected in this document; it should always be consulted with a medical professional beforehand.

ABOUT THIS SUMMARY

SPONSOR: MEDICA SCIENTIA INNOVATION RESEARCH S.L.

TUMOR TYPE: Metastatic Hormone-Naïve Prostate Cancer (mHNPC)

MEDICINE(S) STUDIED: Enzalutamide and Talazoparib

DATES OF STUDY: From October 2020 to May 2022

TITLE OF THIS STUDY: First results from ZZFIRST: a randomized phase II trial of enzalutamide with or without talazoparib in metastatic hormone-naïve prostate cancer

DATE OF THIS REPORT: July 2024

STUDY FUNDER: PFIZER S.L.U

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What was the purpose of this study?

Metastatic hormone-naïve prostate cancer (mHNPC) is a lethal form of prostate cancer that accounts for 50% of prostate cancer deaths. It exhibits significant genomic heterogeneity, often resembling advanced metastatic castration-resistant prostate cancer (mCRPC).

Co-targeting the androgen receptor (AR) and DNA damage repair (DDR) pathways has been shown to be synergistic in phase III trials in mCRPC, but the biological mechanisms driving this antitumor synergism are not fully understood. Given that AR inhibitors are now standard of care in mHNPC, there is interest in testing this combination in this earlier clinical setting.

This study assesses the safety and efficacy of combining talazoparib –PARP inhibitor: a type of targeted cancer drug– and enzalutamide –an AR inhibitor– in patients with or without DDR gene mutations.

What did researchers want to find out?

It is hypothesized that talazoparib, a PARP inhibitor, demonstrates significant antitumor activity, especially in patients with specific gene defects (such as BRCA1, BRCA2, and others) but might not be as effective for those without these defects.

The combination with enzalutamide is expected to extend the benefit of PARP inhibition to a broader patient population and to prolong the clinical benefit of enzalutamide, thereby delaying the need for treatment change upon disease progression.

When and where did the studies take place?

Between October 2020 and May 2022, 54 patients were enrolled across eight hospitals in Spain: 37 in the talazoparib plus enzalutamide arm and 17 in the enzalutamide arm.

What were the results of the study?

The percentage of patients with Prostate-Specific Antigen (PSA) < 0.2ng/mL at month 12 of therapy in talazoparib plus enzalutamide arm was 73% meeting the primary endpoint (95% CI, 55.9%-86.2%, p<0.001), and 64.7% in the control arm.

Median radiographic progression-free survival (rPFS) was not reached for talazoparib plus enzalutamide arm vs 31.1 months for enzalutamide (hazard ratio 0.5, 95% CI 0.2–1.4). The 2-year rPFS rate was 78.5% for talazoparib plus enzalutamide vs 58.8% for enzalutamide. In the talazoparib plus enzalutamide arm, the most common treatment emergent adverse events were fatigue (any grade: 83.8%; G⩾3: 13.5%) and anemia (any grade: 67.6%; G⩾3: 37.8%).

Two patients in the talazoparib plus enzalutamide arm developed acute leukemia after 26.0 and 32.8 months of treatment.

What were the main medical conclusions?

In this interim analysis, talazoparib plus enzalutamide shows promising antitumor activity and predictable toxicity in high volume mHNPC, to be confirmed with longer follow-up; correlative biomarker studies are ongoing.

Where I can find more information?

Your doctor can help you understand more about this study and the results. Speak to your doctor about the treatment options available in your country. You should not make changes to your care based on the results of this or any single study. Keep taking your current treatment unless instructed by your doctor.

For more details, please visit:
https://www.medsir.org/zzfirst-clinical-trial

The full scientific report of this study is available online at:
www.clinicaltrials.gov

Thank you who took part in the study

If you took part in this study, **Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co**, as the Sponsor, extends its gratitude for your participation. This overview will outline the findings of the study. If you have any queries regarding the study or its outcomes, please reach out to the doctor or staff at your study location.

About Oncoclínicas & CO

Oncoclínicas - the largest cancer care group in Latin America - has a specialized, innovative model that focuses on the entire oncology care process, combining operational efficiency, humanized service and high specialization, through a medical team made up of more than 2,600 professionals, who mainly specialize in oncology. With the mission of making cancer treatment accessible to everyone in the country, it offers a complete operational system made up of outpatient clinics integrated with highly complex oncology centers. It currently has 134 units in 35 Brazilian cities, providing access to cancer care in all regions where it operates, with the quality standards of the best cancer centers in the world.

Through technology, precision medicine and genomics, Oncoclínicas ensures effective results and facilitates access to oncology treatment and has performed more than 595,000 treatments in the last 12 months alone. It is the exclusive partner in Brazil of the Dana-Farber Cancer Institute, an affiliate of Harvard Medical School and one of the most prestigious cancer research and treatment centers in the world. The Group also owns Boston Lighthouse Innovation, a bioinformatics company based in Cambridge, USA, and holds shares in MEDSIR, a Spanish company dedicated to the development and management of clinical trials for independent cancer research. The company is also developing projects in collaboration with the Weizmann Institute of Science in Israel, one of the world's most prestigious multidisciplinary scientific and research institutions, whose international board includes Bruno Ferrari, founder and CEO of Oncoclínicas.

For further information: www.grupooncoclinicas.com

ABOUT MEDSIR

Founded in 2012, MEDSIR works closely with its partners to drive innovation in oncology research. Based in Spain and the United States, the company manages all aspects of clinical trials, from study design to publication, utilizing a global network of experts and integrated technology to streamline the process. The company offers proof-of-concept support and a strategic approach that helps research partners experience the best of both worlds from industry-based clinical research and investigator-driven trials. To promote independent cancer research worldwide, MEDSIR has a strategic alliance with Oncoclínicas, the leading oncology group in Brazil with the greatest research potential in South America. Learn how MEDSIR brings ideas to life: www.medsir.org