PRESS RELEASE

Villejuif, 18th July 2025

THE LANCET

A DUAL TREATMENT PROVES ITS EFFICACY IN AN AGGRESSIVE SUBTYPE OF PROSTATE CANCER

Two articles published simultaneously in *The Lancet* present updated results from the TALAPRO-2 clinical trial. Led by Professor Karim Fizazi, Professor at Paris-Saclay University and Head of the Genitourinary Oncology Committee at Gustave Roussy, the trial assesses the combination of a PARP inhibitor with a next-generation hormone therapy in advanced prostate cancer. This approach proved particularly effective in patients with BRCA2 gene alterations.

Metastatic prostate cancers that are resistant to traditional hormone therapies remain incurable and tend to be more aggressive in patients with alterations in DNA repair genes, such as BRCA2. In this subgroup, average life expectancy is around two years.

TALAPRO-2 is a phase III, international, randomised, double-blind clinical trial involving a total of 805 patients with metastatic castration-resistant prostate cancer. Participants were recruited across 200 centres in North America, Europe and the Asia-Pacific region. Among them, 399 patients with DNA repair gene abnormalities were also included in a dedicated cohort.

TALAPRO-2 aimed to evaluate the efficacy of an innovative therapeutic combination: the PARP inhibitor talazoparib paired with enzalutamide, a second-generation hormone therapy. Patients were randomly assigned to two groups:

- One group received a daily oral combination of talazoparib (0.5 mg) and enzalutamide (160 mg).
- The other group received enzalutamide alone (160 mg daily by mouth).

Marked Efficacy in BRCA2 Patients

The results published in *The Lancet* show a particularly pronounced benefit of the talazoparib/enzalutamide combination in patients with a BRCA2 gene mutation.

In this group, after four years of follow-up, median overall survival had not yet been reached for patients receiving both drugs, with more than half of them still alive at the

time of analysis. In contrast, patients receiving hormone therapy alone had a median overall survival of 28.5 months.

“These findings show that in patients with metastatic castration-resistant prostate cancer and BRCA2 gene alterations, the talazoparib/enzalutamide combination can double life expectancy — a remarkable result. TALAPRO-2 also demonstrates that this combination reduces the risk of deterioration in quality of life or the onset of symptoms associated with cancer progression,” explains Professor Karim Fizazi.

Cancer cells with a defective BRCA2 gene already struggle to repair their DNA. Adding a PARP inhibitor to hormone therapy leads to the accumulation of DNA damage in tumour cells, resulting in cell death.

Understanding the Molecular Profile of Tumours

In the overall cohort — including all patients, regardless of whether they had DNA repair gene alterations — adding a PARP inhibitor to next-generation hormone therapy also showed a benefit, albeit to a lesser extent: the median overall survival increased from 37 months (with enzalutamide alone) to 45.8 months (with the talazoparib/enzalutamide combination). The difference was smaller when excluding patients with BRCA2 alterations.

“The updated TALAPRO-2 results highlight the importance of molecular testing in patients with metastatic castration-resistant prostate cancer — particularly to determine the presence of BRCA2 alterations. If such an alteration is identified, patients can be directed towards a combination therapy with a PARP inhibitor and second-generation hormone therapy, which is likely to become the new standard of care for this subgroup,” says Professor Karim Fizazi. *“This molecular testing can be carried out via liquid biopsy by analysing circulating tumour DNA in the blood. It is a highly reliable and informative method, particularly in prostate cancer,”* he concludes.

Sources
The Lancet

Talazoparib plus enzalutamide in men with HRR-deficient metastatic castration-resistant prostate cancer: final overall survival results from the randomised, placebo-controlled phase 3 TALAPRO-2 trial
Published 16th July 2025
DOI: https://doi.org/10.1016/S0140-6736(25)00683-X

Talazoparib plus enzalutamide in men with metastatic castration-resistant prostate cancer: final overall survival results from the randomised, placebo-controlled, phase 3 TALAPRO-2 trial
Published 16th July 2025
DOI: https://doi.org/10.1016/S0140-6736(25)00684-1

About Gustave Roussy

Ranked first in France, first in Europe and fourth in the world, Gustave Roussy is a centre of global expertise entirely dedicated to patients living with cancer. The Institute is a founding pillar of the Paris-Saclay Cancer Cluster. Source of therapeutic innovations and diagnostic breakthroughs, the Institute welcomes nearly 50,000 patients each year, including 3,500 children and adolescents, and develops an integrated approach combining research, care and teaching. An expert in rare cancers and complex tumours, Gustave Roussy treats all cancers at all stages of life. It offers its patients personalised care that combines innovation and humanity, taking into account both care and the physical, psychological and social quality of life. With 4,100 employees at two sites, Villejuif and Chevilly-Larue, Gustave Roussy brings together the expertise essential for high-level cancer research; 40% of treated patients are included in clinical studies. To find out more about Gustave Roussy and follow the Institute's news: www.gustaveroussy.fr/en, X, Facebook, LinkedIn, Instagram and Bluesky.

About Université Paris-Saclay

Formed through the joint ambition of universities, grandes écoles and research organisations, Université Paris-Saclay ranks among Europe's and the world's top universities, spanning the fields of Science and Engineering, Life and Health Sciences, and Social Sciences and Humanities. Its scientific policy closely integrates research and innovation, covering both fundamental and applied science to address major societal challenges. From undergraduate studies to doctoral programmes and grandes écoles pathways, Université Paris-Saclay offers a wide range of academic programmes aimed at student success and employability. It prepares students for a rapidly changing world, where critical thinking, agility and lifelong learning are essential. The University also offers an extensive lifelong learning programme. Located south of Paris, Université Paris-Saclay benefits from strong international visibility and close ties with economic stakeholders — large industrial groups, SMEs, start-ups, local authorities and associations. www.universite-paris-saclay.fr

PRESS CONTACT

GUSTAVE ROUSSY :
Claire Parisel – claire.parisel@gustaveroussy.fr – Tel. +33 1 42 11 50 59 – +33 6 17 66 00 26