

Novel Prostate Cancer Treatment Can Reduce Risk of Disease Progression by Half

Adding Talzenna to Xtandi may help stop the disease from progressing into a more difficult-to-treat stage.

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Takeaways:

- The TALAPRO-3 clinical trial studied a combination therapy that includes enzalutamide [Xtandi], a medication that blocks male hormones from fueling cancer growth, and the drug talazoparib [Talzenna] in patients with metastatic or advanced prostate cancer and certain gene alterations.
- Researchers found that the combination treatment may help stop the disease from progressing into a more difficult-to-treat stage.

Impact: The results of TALAPRO-3 research suggest that earlier intervention with this combination therapy could improve outcomes for men with advanced prostate cancer before the disease becomes resistant to treatment.

A Phase III clinical trial led by [Neeraj Agarwal, MD, FASCO](#), senior director of clinical research at [Huntsman Cancer Institute](#) and professor of internal medicine at the [University of Utah](#) (the U), has found that a combination prostate cancer treatment could prevent the disease from progressing into a harder-to-treat form of cancer in select patients.

The study, TALAPRO-3 ([NCT04821622](#)), evaluated a combination of two drugs—talazoparib and enzalutamide—in patients with metastatic castration-sensitive prostate cancer. This is a form of the disease that has spread beyond the prostate but remains susceptible to standard hormone therapy treatment. The patients involved also had prostate cancer affected by certain gene mutations, including but not limited to BRCA1 and BRCA2 mutations, that often signal more

aggressive disease.

Agarwal and his research team assessed enzalutamide in combination with talazoparib in comparison to enzalutamide alone, the standard of care. Using the two drugs together led to an observed 52% reduction in the risk of disease progression or death.

The results of the trial [have been published](#) in the prestigious New England Journal of Medicine. Agarwal also presented these findings as a late-breaking abstract at the [annual meeting](#) of the [American Society of Clinical Oncology](#).

“Delaying progression to castration-resistant disease, when hormone therapy will no longer work, remains a significant challenge in patients with an earlier stage of metastatic prostate cancer, also known as castration-sensitive prostate cancer. This is especially true for patients with mutations including BRCA1 and BRCA2, who often experience poorer outcomes,” says Agarwal. “With more than three years of follow-up, the novel combination of talazoparib plus enzalutamide demonstrated durable disease control across our patient population.”

Prostate cancer needs male sex hormones, called androgens, to grow. Patients with castration-sensitive prostate cancer can undergo therapies to reduce the levels of androgens like testosterone or to stop the body from producing androgens at all. Androgen deprivation therapy, also known as medical castration, can slow the cancer’s progression. Prostate cancer becomes castration resistant when it no longer slows in response to a drop in testosterone.

Enzalutamide, whose brand name is XTANDI, is an androgen receptor blocker that prevents male hormones from feeding the cancer. Talazoparib is a [PARP inhibitor](#), a drug that stops damaged cancer cells from repairing themselves. Talazoparib is also known by its brand name, Talzenna.

In the TALAPRO-3 patient population, Agarwal and his research team found that talazoparib plus enzalutamide significantly improved radiographic progression-free survival versus the use of only enzalutamide. Radiographic progression refers to the time it takes for a cancer to visibly progress, or worsen, using imaging like CT and bone scans.

After three years, the combination of the two therapies had a radiographic progression-free survival rate of 77%. With enzalutamide alone, it was 56%. The combination also improved progression-free survival rates in patients with BRCA and certain other mutations. These gene alterations are present in approximately 25% to 30% of patients with castration-sensitive metastatic prostate cancer.

“These findings underscore the importance of genetic testing as part of routine care and highlight the potential for talazoparib plus enzalutamide to meaningfully improve the outcomes of patients at this particular point of diagnosis,” says Agarwal. “Once tested, patients with these mutations can start this combination therapy earlier and slow the progression of the disease. This is a pivotal step in personalizing care for prostate cancer patients.”

Agarwal also says that these benefits were achieved without meaningful deterioration in most patient-reported outcomes compared to enzalutamide alone, suggesting that patients may maintain their quality of life while receiving more effective therapy.

TALAPRO-3 enrolled 599 men from 266 locations, both in the United States and abroad. The clinical trial builds on Agarwal's [previous research](#) using the same combination therapy in the treatment of metastatic castration-resistant prostate cancer, the later stage of the disease. That study, called TALAPRO-2, began at Huntsman Cancer Institute in 2017. The novel treatment received U.S. Food and Drug Administration approval in 2023 for metastatic castration-resistant prostate cancer with certain gene alterations.

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