

Could Two Drugs Be Better Than One for Treating Prostate Cancer?

UCSF-led clinical trial shows improved benefit of combination drug therapy without worse side effects.

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Combining testosterone-blocking drugs in patients with prostate cancer relapse prevents the spread of cancer better than treatment with a single drug, a multi-institution, phase 3 clinical trial led by UC San Francisco researchers has found.

The approach can extend the time between debilitating drug treatments without prolonging the time it takes to recover from each treatment.

Prostate cancer affects 1 in 8 men and causes 34,000 deaths each year in the United States. It is usually treated with one of several testosterone-lowering drugs for a set period of time.

“This adds to a growing body of evidence in favor of more intensive testosterone-blocking therapy in patients with higher-risk prostate cancer,” said [Rahul Aggarwal](#), MD, professor in the UCSF School of Medicine and lead author of the paper.

The researchers’ findings were published on Jan. 23, 2024, in the [Journal of Clinical Oncology](#). They were first announced in September 2022 at the annual meeting of the European Society for Medical Oncology.

A case for intensifying prostate cancer treatment

The new study focused on patients who had surgery for prostate cancer, and yet the cancer relapsed and was detected through a sudden jump in the blood levels of a protein called prostate-specific antigen (PSA).

“We looked at patients who had a fast rise in their PSA — an indicator of a higher-risk form of relapsed prostate cancer,” Aggarwal said. “Our goal was to test several different hormone therapy strategies to find the best approach in terms of delaying the cancer’s progression.”

Between 2017 and 2022, 503 patients were randomly assigned to take a single testosterone-lowering therapy chosen by their oncologist, or to combine it with one or two other testosterone-

lowering drugs. The additional drugs were already FDA-approved for other cancers but hadn't been tested in this way with prostate cancer.

The patients stayed on the assigned therapy for a year. Whether given singly or in combination, the drugs caused their testosterone to plummet. That put the brakes on their cancer but also caused fatigue, hot flashes, decreased libido and other problems for patients, according to Aggarwal.

Compared to the prostate cancer patients who only received a single drug therapy during their year of treatment, patients who received either one or two additional drugs stayed cancer-free, with low PSA levels, for longer.

Once off the treatment, patients who took the combination therapies saw their testosterone levels recover just as fast as others who took the single drug.

The researchers are following up with a more detailed analysis of how patients fared on the different treatments — which side effects they experienced and for how long, and how they felt overall as they recovered.

“New cancer therapies must clear a high bar to make their way to patients,” Aggarwal said. “With the evidence in this study and others, combination hormone therapy should be considered a standard of care in prostate cancer patients with high-risk relapse after prior treatment.”

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