New Therapy Delays Progression of Recurrent Prostate Cancer

Adding PSMA-targeting radioligand therapy to stereotactic body radiotherapy more than doubled progression-free survival in men with recurrent prostate cancer.

October 2, 2025 By UCLA Health

Patients with recurring prostate cancer who were treated with a new PSMA-targeted radioligand therapy before stereotactic body radiotherapy (SBRT) went more than twice as long without their disease worsening compared with those who received SBRT alone, according to new clinical trial results from UCLA Health Jonsson Comprehensive Cancer Center researchers.

Findings from the trial presented [September 28] at the 2025 American Society for Radiation Oncology Annual Meeting in San Francisco, showed that men who received the radioligand drug went a median of 17.6 months without disease progression, compared with 7.4 months for those who received SBRT alone. This translated into a significant delay in the start of hormone therapy, which is often used to treat recurrent disease.

“This is the first randomized trial to show that PSMA-targeting radioligand can significantly delay progression when added to metastasis-directed radiation,” said Dr. Amar Kishan, executive vice chair of radiation oncology at the David Geffen School of Medicine at UCLA and first author of the study. “It gives patients more time before needing hormonal therapy, which can carry significant side effects such as fatigue and bone loss. Avoiding or delaying hormonal therapy consistently benefits quality of life. Moreover, the trial results establish that radioligand therapy agents, which thus far have only been studied in more advanced disease, have a role to play earlier in the disease course.”

Prostate cancer is the second most common cancer among men worldwide. For some, the disease returns years after initial treatment in only a handful of new lesions, a stage known as oligorecurrent disease.

SBRT has become an increasingly common approach for treating these cases, targeting the visible lesions while sparing surrounding healthy tissue. While the approach can delay progression and postpone the need for hormone therapy, most men eventually relapse, often because of microscopic disease too small to detect on imaging scans. Radioligand therapy, which precisely delivers radiation to cancer cells while minimizing harm to healthy tissues, may help address this hidden disease.

The Phase 2 study, called the LUNAR trial, explored whether adding a radioactive drug called PNT2002 — a molecule that specifically targets PSMA, a protein highly expressed on the surface of prostate cancer cells — before SBRT could help control these hidden tumors.

“This trial is especially exciting because it showcases the full potential of PSMA-based theranostics technologies,” said senior author of the study Dr. Jeremie Calais, director of the Ahmanson Translational Theranostics Division’s clinical research program and associate professor at the department of molecular and medical pharmacology at the David Geffen School of Medicine at UCLA “We leveraged PSMA PET imaging technology to guide SBRT targeting, which is more precise than other imaging methods. And we combined it with PSMA radioligand therapy to treat PSMA expressing sites of disease, both the ones visible by PET but also the microscopic sites too small to be detected by PET.”

To test this hypothesis, the researchers enrolled 92 men with recurrent prostate cancer into the trial and split them at random into two groups. One got SBRT alone, the other got two doses of 177Lu-PNT2002 drug first, then SBRT. The team tracked patients with regular PSA blood tests and PSMA PET scans to see how long they stayed free of cancer progression.

They found adding 177Lu-PSMA before SBRT more than doubled progression-free survival, extending it from 7.4 months to 17.6 months, reducing the risk of cancer returning, the need for hormone therapy, or death by 63%. These benefits were seen across all patient subgroups, regardless of disease stage or the number of lesions, with minimal side effects. Additionally, men in the combination arm went a median of 24.3 months before starting hormonal therapy, compared with 14.1 months in the SBRT-only group.

The team also identified biological markers that may help predict which patients will benefit most from treatment. A stronger immune response after SBRT, measured by T cell receptor changes, was linked to better outcomes, and a set of 20 genes associated with immune function and DNA repair helped define patients at higher or lower risk of progression.

Despite the clear benefit of adding 177Lu-PNT2002 to SBRT, 64% of men still experienced disease progression, underscoring that microscopic cancer remains a major challenge, the researchers noted.

“This is an important proof of principle,” said Kishan, who is also the co-director of the cancer molecular imaging, nanotechnology and theranostics program at the UCLA Health Jonsson Comprehensive Cancer Center. “It suggests we may be able to intervene earlier with radioligand therapy and meaningfully change the course of disease. And, importantly, we didn’t see significantly worse side effects with the addition of the drug. Further research is needed to track longer-term outcomes, and we will also be actively looking at other ways of optimizing response rates.”

“This work is a great example of true collaboration between radiation oncology and nuclear medicine, leveraging theranostics at its best, a mix of imaging and therapy,” Calais added.

The study was funded by Lantheus.

This news release was published by UCLA Health on September 28, 2025.
