

# **New radiopharmaceutical shows antitumor activity in patients with advanced prostate cancer**

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Researchers at Weill Cornell Medicine have led a phase 1 trial of a new drug that delivers potent radiation therapy directly and specifically to

cancer cells in patients with advanced prostate cancer. The clinical trial showed that the "radiopharmaceutical" was well tolerated and demonstrated promising antitumor activity, according to a new study published on Nov. 2 in the *Journal of Clinical Oncology*.

The radiopharmaceutical 225Ac-J591 was administered in a single injection and consists of two parts: an antibody that helps find the [cancer cells](#) is linked to a molecule that delivers a deadly dose of radiation. Specifically, an antibody named J591 that targets a protein found on the surface of most prostate cancer cells called prostate-specific membrane antigen (PSMA), is linked to the radioactive isotope actinium-225, which emits high-energy alpha particles to destroy cancer cells. Dr. Neil Bander, professor emeritus of urology at Weill Cornell Medicine, developed J591 in 1996. This antibody targets prostate cancer cells anywhere in the body while avoiding healthy tissues and organs.

"Despite considerable advances to improve prostate cancer survival, there is no cure yet for metastatic prostate cancer," said lead author and principal investigator of the trial Dr. Scott Tagawa, a professor of medicine and medicine in urology at Weill Cornell Medicine and medical director of the genitourinary oncology program at NewYork-Presbyterian/Weill Cornell Medical Center. "Our results from this first-in-human study of a PSMA-targeted alpha emitter are very exciting and a testament to more than two decades of translational research at Weill Cornell Medicine."

Prostate cancer is the second most common cause of death due to cancer in men in the United States. For those whose cancer has spread (metastasized) to other areas of the body and does not respond to therapies that lower testosterone, the five-year survival rate is 34 percent, according to the American Cancer Society.

## **Advantages of using a drug that emits alpha particles**

Previously, scientists at Weill Cornell Medicine radiolabeled J591 with beta particle emitters, such as lutetium-177 ( $^{177}\text{Lu}$ ). In previous phase 1 and 2 studies,  $^{177}\text{Lu}$ -J591 effectively targeted metastatic sites with acceptable toxicity and showed encouraging signs of response and improvements in overall survival.

Dr. Bander's lab has also investigated J591 attached to another molecule called actinium which emits alpha particles. "Actinium is about four thousand times more potent and has a shorter delivery range than lutetium, delivering more energy to kill cancer cells with less harm to surrounding healthy tissue," Dr. Tagawa said.

With the need for more [treatment options](#), Dr. Tagawa conducted the phase 1 study of  $^{225}\text{Ac}$ -J591 between October 2017 and January 2021 at Weill Cornell Medicine and Tulane University School of Medicine. A total of 32 patients with metastatic prostate cancer received a single injection of the radiopharmaceutical: 22 patients received one of seven escalating dose levels, and then 10 patients in the expansion group received the highest dose.

## Promising phase 1 trial results

The researchers found  $^{225}\text{Ac}$ -J591 had good antitumor activity against advanced metastatic prostate cancer and was well tolerated. Prostate-specific antigen (PSA)—an indication of [cancer](#) severity—decreased by at least half for 47 percent of patients. In addition, 13 of 22 (59 percent) patients experienced a drop in circulating tumor count. These results are encouraging signs that the treatment was working to destroy [prostate cancer](#) cells.

Most high-grade adverse events involved low blood cell counts, and all were temporary. As the highest dose level of  $^{225}\text{Ac}$ -J591 that could be

given without [severe side effects](#) was not reached and only one dose was administered in the phase 1 trial, a follow-up combined phase 1/phase 2 study is now underway. The new study will further assess its safety and efficacy with split or multiple infusions at higher cumulative doses.

"These strong results are due to the multidisciplinary collaboration between medical oncologists and our nuclear medicine group," said Dr. Tagawa, co-leader of the Experimental Therapeutics Program at the Sandra and Edward Meyer Cancer Center and a member of the Englander Institute of Precision Medicine. "We look forward to continuing to advance 225Ac-J591 in a combined phase 1/phase 2 follow-up study and future trials. If successful, 225Ac-J591 may offer new hope for patients with [metastatic prostate cancer](#)."

Cornell University has exclusively licensed this technology to Convergent Therapeutics, Inc., a clinical stage pharmaceutical company focused on developing next-generation radiopharmaceutical therapies for [prostate](#) and other cancers.

**More information:** Scott T. Tagawa et al, Prostate-Specific Membrane Antigen–Targeting Alpha Emitter via Antibody Delivery for Metastatic Castration-Resistant Prostate Cancer: A Phase I Dose-Escalation Study of 225Ac-J591, *Journal of Clinical Oncology* (2023). DOI: 10.1200/JCO.23.00573 , [doi.org/10.1200/JCO.23.00573](https://doi.org/10.1200/JCO.23.00573)

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