

Molecularly targeted radiation therapy extends survival for patients with advanced prostate cancer

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Dr. Oliver Sartor, co-principal investigator of the VISION clinical trial, explains how molecularly targeted radiation therapy works and how it could change the landscape of treatment options for patients with advanced prostate cancer. Video by Carolyn Scofield.

A new cancer treatment that uses engineered radioactive molecules to target prostate cancer cells and inhibit tumor growth extended survival for patients with advanced prostate cancer, according to newly announced results of the [VISION trial](#).

The international phase III clinical trial, which was co-led by Tulane University medical oncologist [Dr. Oliver Sartor](#), is the first to use this approach to demonstrate improvements in survival for prostate cancer patients.

Researchers compared ^{177}Lu -PSMA-617, a targeted radioligand therapy, against the current standard of care for men with metastatic castration-resistant prostate cancer (mCRPC). Radioligand therapy combines a targeting compound that binds to markers expressed by tumors and a radioactive isotope, causing DNA damage that inhibits tumor growth and replication. This approach enables targeted delivery of radiation to the tumor, while limiting damage to the surrounding normal tissue.

The trial is widely regarded as the most important demonstration of radioligand therapy's efficacy in patients being treated for cancer, said Sartor, Medical Director of Tulane Cancer Center and C. E. and Bernadine Laborde Professor of Cancer Research at Tulane University School of Medicine.

"These are exceptionally strong data. This practice-changing trial is unequivocally important because it demonstrates an improvement in overall survival for patients who have very few alternative treatment options," Sartor said. "Furthermore, the therapy is exceptionally well tolerated with a low incidence of significant side

effects”

Sartor was co-principal investigator on the trial along with Dr. Bernd Krause, of Germany’s Rostock University Medical Center. The trial was sponsored by Endocyte Inc., a Novartis company. Sartor is senior author of the abstract that will be presented on June 6 at the annual meeting for the American Society of Clinical Oncology.

VISION enrolled 831 mCRPC patients at 87 sites in 10 countries. All had been previously treated with chemotherapy and conventional hormonal therapy – either abiraterone or enzalutamide – and still had progressive disease. Prospective participants also underwent ^{68}Ga -PSMA-11 PET scans to determine eligibility for randomization in the trial. Prostate-specific membrane antigen (PSMA) is a unique protein found on the surface of most prostate cancer cells. The experimental agent tested in VISION – ^{177}Lu -PSMA-617 – is an engineered radioactive molecule that binds to PSMA and delivers therapeutic doses of radiation to the prostate cancer cells. A total of 87% of scanned patients were PSMA-positive and considered eligible for the trial.

Trial participants were randomized into either the standard of care arm or the experimental arm, where ^{177}Lu -PSMA-617 (in addition to standard of care) was given every 6 weeks for four planned doses. Up to six doses could be administered for responding patients. The standard of care choice was up to the investigator, but no chemotherapy or other isotopes were allowed.

After a median 20.9 months of follow-up, the study showed that ^{177}Lu -PSMA-617 plus standard of care significantly improved median survival (15.3 vs. 11.3 months) versus standard of care alone. Tumors were more likely to shrink and PSA values were more likely to fall in those patients that received the molecularly targeted radiation.

“The therapy is well tolerated, and we’ve had some dramatic responses,” said Sartor, who anticipates approval of this new agent by regulatory agencies across the world, including the U.S. Food and Drug Administration, within the next year.

Next steps following this proof of principle trial, according to Sartor, are to test the agent in less heavily pre-treated patients, including those diagnosed with metastatic

prostate cancer and no prior hormonal treatments.

“This is an important new therapy. I envision that it will be used earlier in the stages of disease and new clinical trials are working on that issue right now,” Sartor said