Novel radioligand therapy proven superior for metastatic prostate cancer patients

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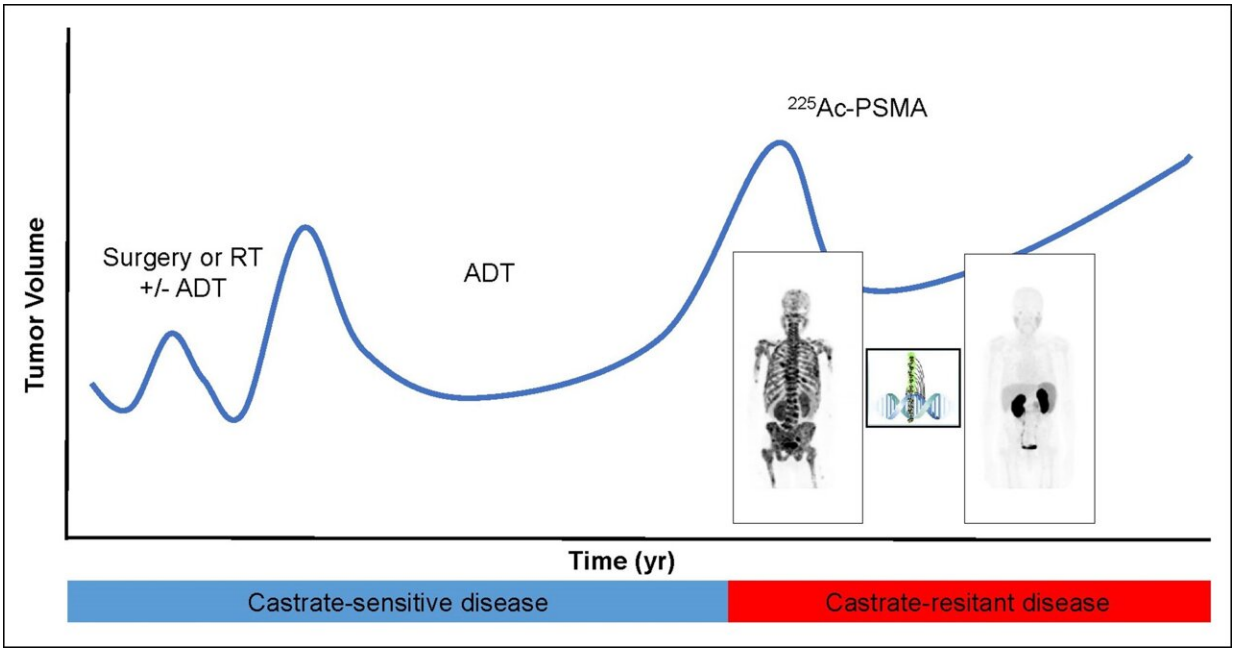

Current known landscape of treatment of prostate cancer, with ^{225}Ac-PSMA as potential option in men who develop mCRPC after ADT. Credit: *Journal of Nuclear Medicine* (2022). DOI: 10.2967/jnumed.121.263618

A novel prostate cancer treatment—^{225}Ac-PSMA-617 radioligand therapy—has been shown to increase the progression free survival (PFS) and overall survival (OS) of metastatic castration-resistant prostate cancer (mCRPC) patients, according to research published by *The Journal of Nuclear Medicine*. Ninety-one percent of patients experienced

a greater than 50% reduction of their initial PSA (prostate specific antigen) value after treatment with ^{225}Ac-PSMA-617, resulting in a PFS of 22 months and an OS not yet reached at the conclusion of the study.

While the five-year survival rate of localized prostate cancer is nearly 100%, for mCRPC patients it is only 30%. Clinical studies have demonstrated the efficacy and safety of several therapies, including ^{177}Lu-PSMA in the post- androgen deprivation therapy (ADT) setting in patients with mCRPC. Additional therapies, such as ^{225}Ac-PSMA-617, are often considered once the disease begins to progress again.

"Previous research has shown a remarkable therapeutic efficacy of ^{225}Ac-PSMA-617 in heavily pre-treated mCRPC patients, as demonstrated by the initial work from Kratochwil et al. from Germany," said Mike Sathekge, professor and head of the Nuclear Medicine Department at the University of Pretoria and Steve Biko Academic Hospital in Pretoria, South Africa. "In this study we sought to compare ^{225}Ac-PSMA-617 to other common post-ADT treatments, such as chemotherapy, enzalutamide, and abiraterone acetate or docetaxel, administered in a comparable setting."

The retrospective study included 53 patients who received ^{225}Ac-PSMA-617 directly following ADT therapy. Molecular imaging with ^{68}Ga-PSMA PET/CT was obtained at baseline, before every treatment cycle, and on follow-up for select patients to determine how much ^{225}Ac-PSMA-617 to administer and for response assessment. Patients' PSA levels were also obtained to assess response.

In the patients who experienced a PSA decline of more than 50%, the median PFS was 22 months, and the OS was not yet reached at the end of the study (55 months). For those with a PSA decline of less than 50%, the median PFS was four months, and the OS was nine months. In total, 48 patients (91%) had a PSA decline of more than 50%. Additionally,

PET imaging became negative (showing no signs of disease) in 30 patients.

"It is clear that ^{225}Ac-PSMA-617 is an effective treatment for men with mCRPC," noted Sathekge. "This radioligand therapy may be a viable treatment option, especially if standard of care options are not available or are contraindicated. Since ^{225}Ac-PSMA-617 has few treatment-related toxicities (notably xerostomia), it could also prove helpful in low middle income countries where patients are more likely to refuse chemotherapy or the current standard of care due to fear of side effects."

This study was made available online in February 2022 in the *The Journal of Nuclear Medicine*.

More information: Mike Sathekge et al, mCRPC patients receiving ^{225}Ac-PSMA-617 therapy in post androgen deprivation therapy setting: Response to treatment and survival analysis, *Journal of Nuclear Medicine* (2022). DOI: 10.2967/jnumed.121.263618

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