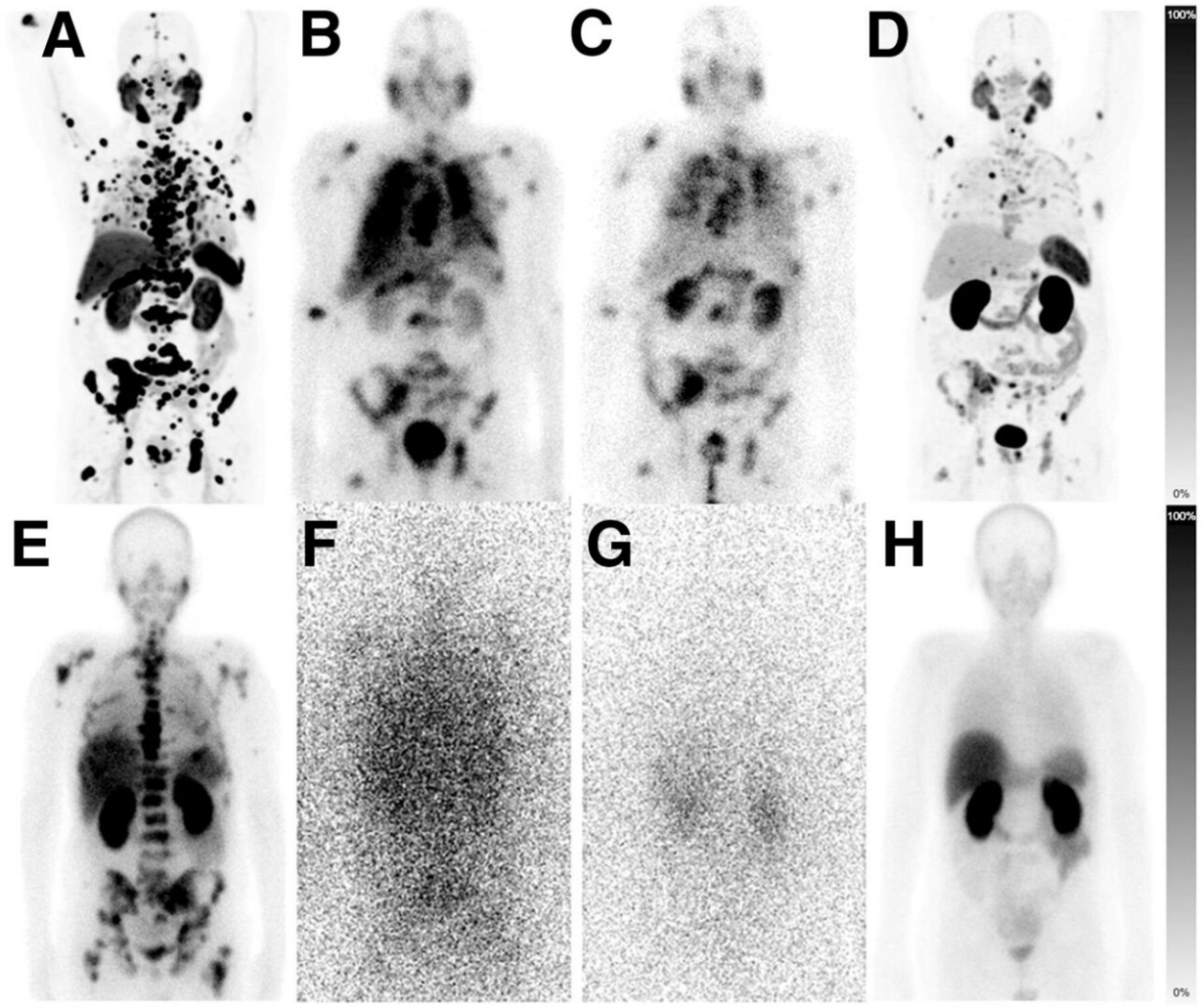
Lower dose prostate cancer treatments found to retain efficacy while improving tolerability

July 24 2024



(A–D) Patient with meningeal, adrenal, pulmonary, lymph nodal, and osseous metastases. Credit: H Rathke and C Kratochwil, et al., Department of Nuclear Medicine, Heidelberg University Hospital, Heidelberg, Germany.

Two reduced dose radiopharmaceutical therapy approaches for advanced stage metastatic castrate-resistant prostate cancer have been shown to be just as effective as the standard dose, according to new research published in the July issue of *The Journal of Nuclear Medicine*.

Treatment with deescalated ^{225}Ac-PSMA-617 or a cocktail therapy of ^{177}Lu/^{225}Ac-PSMA-617 resulted in similar median overall survival and prostate specific antigen (PSA) response rates as the standard ^{225}Ac-PSMA-617 dose and was better-tolerated among patients.

The standard dose for ^{225}Ac-PSMA targeted radiopharmaceutical alpha-therapy is 100 kBq per kilogram of body weight or an approximation of eight MBq. After multiple treatment cycles of this dose, salivary gland toxicity often increases and patients experience uncomfortable dry mouth. For some patients, this impact on their quality of life causes them to discontinue treatment.

"Preliminary data from other studies has shown that reduced doses of PSMA treatment result in lower rates of dry mouth while still maintaining promising anti-tumor activity," said Hendrik Rathke, MD, from the Department of Nuclear Medicine at Heidelberg University Hospital in Heidelberg, Germany.

"In our study we aimed to determine the tolerability, PSA response rate, and overall survival observed in patients who received a regimen of less than 100 kBq of ^{225}Ac-PSMA or an ^{177}Lu/^{225}Ac-PSMA-617 cocktail therapy."

Researchers conducted a retrospective analysis of 233 patients who were treated with ^{225}Ac-PSMA at Heidelberg University Hospital from 2014-2022; 104 received a median of six MBq of ^{225}Ac-PSMA

monotherapy and 129 received an ^{177}Lu/^{225}Ac-PSMA-617 cocktail therapy. Baseline characteristics, PSA response, and overall survival were compared with the most appropriate historical controls.

Of the patients who received ^{225}Ac-PSMA monotherapy, 55 patients (53%) presented with a best PSA response of at least 50%. In the ^{177}Lu/^{225}Ac-PSMA-617 cocktail group, a best PSA response of at least 50% was observed in 74 patients (57%). The median overall survival was nine months in the ^{225}Ac-PSMA monotherapy and was 15 months in the ^{177}Lu/^{225}Ac-PSMA-617 cocktail group. If adjusted for prognostic baseline characteristics, the efficacy of both regimens was not significantly different.

"The baseline prognostic characteristics of patients in this study are worse than patients who were recruited to the VISION clinical trial, yet the median overall survival and PSA response rates are equivalent," noted Rathke. "This leads to the assumption that patients with late stage prostate cancer can benefit from targeted radiopharmaceutical alpha-therapy."

More information: Hendrik Rathke et al, Deescalated225Ac-PSMA-617 Versus177Lu/225Ac-PSMA-617 Cocktail Therapy: A Single-Center Retrospective Analysis of 233 Patients, *Journal of Nuclear Medicine* (2024). DOI: 10.2967/jnumed.123.267206