A novel radionuclide treatment for hormone refractory metastatic prostate cancer

Prostate cancer is the second most common male cancer worldwide and the fourth most common cancer overall. In patients with localized prostate cancer, the five-year survival rate approximates to 100%; however, in patients with distant metastases, it drops to 31%. Almost all patients with metastatic prostate cancer will initially respond to hormone therapy. However, progression to hormone-independent prostate cancer is the main cause of death. Prostate-specific membrane antigen (PSMA) is a surface protein that is normally present on healthy prostate cells, but is found at much higher levels on prostate cancer cells; therefore, PSMA is an attractive target for diagnosis and therapy of metastatic prostate cancer.

PSMA-617, which was developed in Heidelberg, Germany, is a small molecule that is capable of specifically attaching to PSMA and can be labeled with various radioactive tracers for diagnostic imaging (e.g. ^{68}Ga-PSMA PET/CT) and therapy (^{177}Lu-PSMA-617). It is a clever substance, because it can bind to prostate tumor cells, independent of their locations in the body (e.g. in bone, lymph nodes or liver).

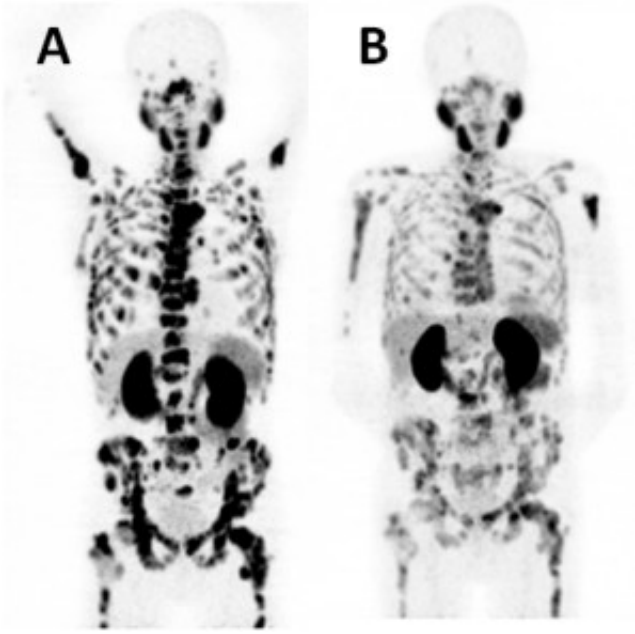

Fig. 1. A: ^{68}Ga-PSMA PET shows diffuse bone metastasis in a 75-year-old patient (normally in a patient without bone metastases the bones cannot be seen, because they do not have any PSMA expression). The PSA was prior to injection with 1160 ng/ml. B: PET scan two months after treatment shows an eye-catching reduction of PSMA expression correlated with PSA decline to 71 ng/ml. The patients did not experience any side-effects or blood toxicity.

Here, we analyzed the early side-effects and the response rate in the first 10 patients (62 to 81 years old), who received therapy with ^{177}Lu-PSMA. All of them were hormone-resistant, and five of them had received chemotherapy, too. All of them had multiple bone and lymph node metastases with increasing PSA under hormone therapy. After a ^{68}Ga-PSMA PET scan, which confirmed the PSMA expression on tumor cells, the patients received ^{177}Lu-PSMA-617 as an intravenous injection. No patient experienced any side-effects immediately after injection of tracer. No significant change in blood pressure or body temperature was observed. Two patients experienced mild nausea, one of whom had one episode of vomiting. Otherwise, the patients tolerated the therapy very well. We controlled the blood parameters as well as renal and liver function tests every two weeks up to two months after therapy. Apart from one patient, who had received a blood transfusion prior to this therapy, no patient showed any relevant changes in the blood cell counts. There was no relevant negative change of renal or liver parameters.

Two patients complained of fatigue and two other patients complained of dry lips in the first two weeks only. No patient experienced a negative change in performance status. Eight weeks after the therapy seven patients (70%) experienced a PSA decline, of whom six experienced more than 30% and five more than 50% (Fig. 1). This was a remarkable response by patients who normally did not have any other treatment option.

In conclusion, we have shown that a single dose of ^{177}Lu-PSMA-617 for the treatment of metastatic prostate cancer without any other therapy option is safe and seems to have a low early side-effects profile with evidence of positive response to the therapy as evidenced by PSA decline in 70% of patients.

Hojjat Ahmadzadehfar, MD, MSc

Head of therapy section, Department of Nuclear Medicine
University Hospital Bonn, Germany

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Early side effects and first results of radioligand therapy with (177)Lu-DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-centre study.
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