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^{177}Lu-PSMA radioligand therapy for metastatic castration-resistant prostate cancer

SHORT CASE REPORT

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Background

Treatment of castration-resistant metastatic prostate cancer with [^{177}Lu]PSMA radioligand.

Case presentation

A man in his seventies with metastatic prostate cancer received castration therapy for four years, developing castration-resistant disease. PET/CT with [^{68}Ga]PSMA-11 showed high uptake in metastatic lymph nodes. The patient

received 7.4 GBq [^{177}Lu]PSMA-I&T (Curium, Finland) as five treatments at five-week intervals. Five weeks after the first treatment, p-PSA dropped from 154 to 53 µg/L. Five weeks after the fifth treatment, p-PSA was 1.8 µg/L. [^{68}Ga]PSMA-11 PET/CT showed significant reduction in the size of metastases, with the largest decreasing in diameter from 10 to 4 mm. Seven months after the fifth treatment, p-PSA increased to 14.3 µg/L, and [^{68}Ga]PSMA-11 PET/ CT revealed additional skeletal metastases, while the lymph node metastases remained unchanged. Thus, the treatment had a good but temporary effect on the metastases.

Interpretation

Treatment with [^{177}Lu]PSMA radioligand resulted in a temporary regression of the metastases.

Following treatment for rapidly progressing metastatic castration-resistant prostate cancer with ^{177}Lu-PSMA radioligand therapy under Norway's compassionate use programme, significant reduction of the metastases was observed on PET/CT. The therapeutic effect was transient.

A man in his seventies with rapidly progressing metastatic prostate cancer had received castration therapy for four years and developed castration-resistant disease. He had also had a positive response and good tolerance to abiraterone tablets over a period of 3.5 years (daily dose 1000 mg together with prednisolone 10 mg to reduce adverse effects). Abiraterone was discontinued when disease progression was observed with rising prostate-specific antigen (PSA) levels and new lymph node metastases. Chemotherapy was initiated with docetaxel (intravenous infusion 50 mg/m^2 every 2 weeks), which caused intolerable adverse effects, leaving no other treatment options available. In accordance with guidelines, the patient continued endocrine therapy in the form of LHRH analogue with subcutaneous goserelin injections (10.8 mg every three months).

PSA in plasma (p-PSA, reference range 0–4.0 µg/L for men ≥ 60 years) was 154 µg/L and the PSA doubling time was 4.5 months. PET/CT with the Gallium-68-labelled radiopharmaceutical tracer prostate-specific membrane antigen radioligand (PSMA-RL) ([^{68}Ga]PSMA-11) revealed high uptake in scattered metastatic lymph nodes in the pelvis, abdomen, chest and neck, as well as a solitary bone metastasis in the right clavicle (Figure 1). The uptake indicated possible suitability for treatment with Lutetium-177 (a beta-emitting radionuclide) PSMA radioligand therapy ([^{177}Lu]PSMA-RL).

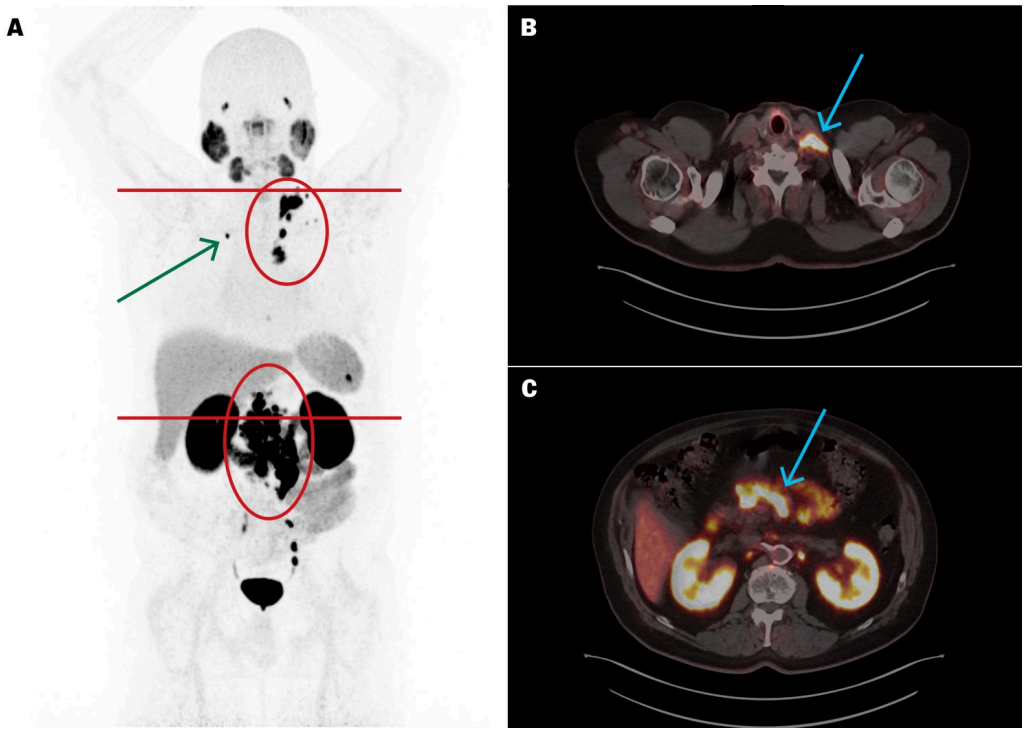

Figure 1 [^{68}Ga]PSMA-11 PET/CT before treatment with [^{177}Lu]PSMA-617 showed high uptake in scattered metastatic lymph nodes in the abdomen, chest and below the left side of the neck (red ring and blue arrow) and in a small skeletal metastasis in the right clavicle (green arrow). High uptake in a small lesion in the spleen was a known haemangioma. Physiological uptake in the salivary glands, kidneys and bladder was also observed.

The treatment is not approved in Norway and was therefore administered under the compassionate use programme. A total of 7.4 GBq [^{177}Lu]PSMA-I&T (Curium, Finland) was administered in five treatments five weeks apart. Five weeks after the first treatment, p-PSA had dropped to 53 µg/L.

Five weeks after the fifth course of treatment, p-PSA was 1.8 µg/L. [^{68}Ga]PSMA-11 PET/CT revealed a significant reduction in the size of metastases (Figure 2), with the largest (target lesion) decreasing in diameter from 10 to 4 mm. Apart from decreased appetite and constipation, the treatment was well tolerated without affecting renal, salivary gland or bone marrow function.

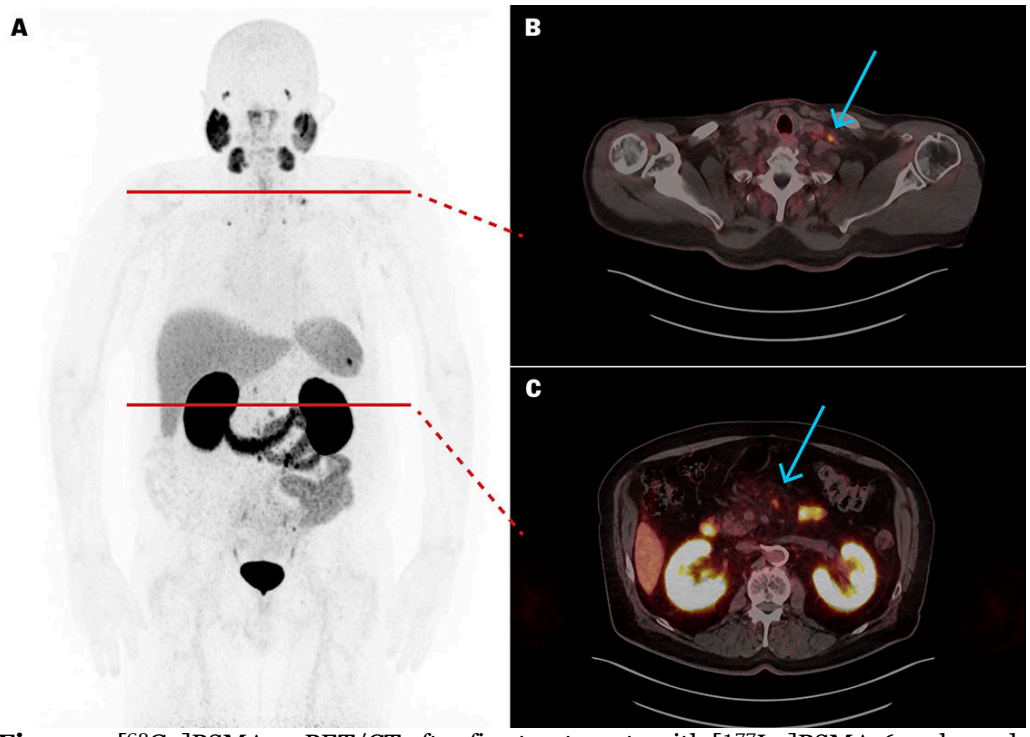

Figure 2 [^{68}Ga]PSMA-11 PET/CT after five treatments with [^{177}Lu]PSMA-617 showed a significant reduction in the size of metastases in the lymph nodes in the abdomen, chest and neck.

Seven months after the fifth treatment, p-PSA had risen to 14.3 µg/L and [^{68}Ga]PSMA-11 PET/CT revealed new small skeletal metastases with high uptake, while lymph node metastases remained unchanged. The treatment thus had a good but temporary therapeutic effect on the metastases.

Discussion

Treatment with [^{177}Lu]PSMA-RL is based on the ligand binding to PSMA cell membrane receptors. A prerequisite for the treatment is therefore a high number of PSMA receptors in the prostate cancer cells, and this is assessed beforehand with [^{68}Ga]PSMA-11 PET/CT (1, 2). After binding to a PSMA receptor on the cell surface, the antigen-ligand complex is internalised in the cell, and this is followed by internal radiation with the beta particles emitted from Lutetium-177. The concentration of energy deposition is high enough to cause considerable radiation damage to DNA and subsequent death of the cancer cells, with low-degree damage to normal surrounding tissue. Renal excretion and physiologically high uptake in salivary glands expose the kidneys and salivary glands to risk, but the standard treatment our patient received is reported to be well tolerated with seldom severe adverse effects (1).

To evaluate response, p-PSA is measured, and CT and/or [^{68}Ga]PSMA-11 PET/CT are/is repeated. A randomised phase 3 trial (VISION) showed that treatment with [^{177}Lu]PSMA-617 (Pluvicto) in addition to standard treatment prolonged overall survival (median 15.3 months) compared to standard treatment alone (median 11.3 months) (1).

Both [^{68}Ga]PSMA-11 and [^{177}Lu]PSMA-RL target PSMA cell membrane receptors, thus forming what is called a theranostic pair. Theranostics is a portmanteau of therapeutics and diagnostics, and describes the coupling of a diagnostic biomarker and a therapeutic agent that have a common target, as seen here with PSMA.

Expectations are high for ongoing trials investigating treatment efficacy in combination with specific pharmaceuticals and treatments administered at an earlier stage of the disease than in the VISION trial (3, 4).

Our patient was not, however, treated with [^{177}Lu]PSMA-617, but [^{177}Lu]PSMA-I&T. The moiety that binds to the PSMA receptor is identical, and the only difference lies in the moiety that binds together the receptor substrate and the moiety that binds Lutetium-177. Trials have shown equal treatment efficacy for the two medications (5).

This case report describes one of the two patients we are aware of who have been treated with [^{177}Lu]PSMA-RL in Norway under the compassionate use programme. Selected patients have received the treatment abroad (primarily in Germany and Finland), where costs have been covered by the Norwegian Health Economics Administration (HELFO) (upon approval by the Office for Treatment Abroad), or they have been privately funded.

Treatments with [^{177}Lu]PSMA-RL have been introduced in the United States, Australia and several countries in Europe. The pharmaceutical was approved by the European Medicines Agency in December 2022. The Norwegian Institute of Public Health published a health technology assessment in June 2023 (6). In January 2024, Norway's Decision Forum decided against its introduction in the country as 'there is no evidence that clinical benefit justifies the cost' (7). However, the Norwegian Hospital Procurement Trust is called on to resume price negotiations with the supplier, and if new information and results emerge, this decision can be reconsidered (7).

The patient has consented to publication of this article.

The article has been peer-reviewed.

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