European Journal of Nuclear Medicine and Molecular Imaging (2019) 46:2212–2213
https://doi.org/10.1007/s00259-019-04410-8

IMAGE OF THE MONTH

Exceptional 4-year response to ^{177}Lu-PSMA radioligand therapy in metastatic castration-resistant prostate cancer

Andrei Gafita[1] · Hui Wang[1] · Robert Tauber[2] · Calogero D'Alessandria[1] · Wolfgang A. Weber[1] · Matthias Eiber[1]

Received: 30 March 2019 / Accepted: 18 June 2019 / Published online: 4 July 2019

^{177}Lu-Prostate-specific membrane antigen (^{177}Lu-PSMA) radioligand therapy (RLT) has demonstrated encouraging efficacy in patients with metastatic castration-resistant prostate cancer (mCRPC) [1]. Furthermore, rechallenge with ^{177}Lu-PSMA has been described as a potential therapeutic option in patients with an excellent response during initial RLT treatment [2].

We report an exceptional response in a 75-year-old patient with mCRPC who underwent 16 cycles of ^{177}Lu-PSMA under a compassionate use programme over 50 months that included the initial treatment and three rechallenge series, each comprising four RLT cycles. ^{68}Ga-PSMA11 PET/CT scans were performed and images were quantified using qPSMA software (SUV-threshold of 3 for bone metastases and a liver-based threshold for soft-tissue lesions) [3]. For the treatment of mCRPC, the patient had already received abiraterone, docetaxel, enzalutamide and ^{223}Ra-dichloride. Serum PSA levels (nanograms per millilitre) are displayed at the bottom of the images. At baseline, the patient presented with diffuse bone marrow carcinomatosis (**a**), but still with an ECOG performance status of 0 that remained constant during the entire treatment. After the initial treatment, a complete response was achieved (**b**). The first rechallenge treatment was performed due to disease recurrence in the rib and sacrum (**c**) after a treatment-free period of more than 1 year, with a further excellent response (**d**). After a 4-month treatment break (**e**), the second rechallenge resulted in only a partial response (**f**). Finally, during the third rechallenge the disease extended to the lymph nodes and pleura, with radiographic progressive disease but still with a biochemical response (**g**, **h**). According to the Common Terminology Criteria for Adverse Events v5.0, grade 1 thrombocytopenia and kidney function impairment developed late during the third rechallenge.

Notably, as with other antitumour regimens, the response decreased with every course of treatment, finally leading to the occurrence of new lesions under therapy and low-grade toxicity. It is assumed that this pattern occurs because of the slow development of resistance. Nevertheless, identifying patients who will tolerate multiple RLT cycles with a sustained therapeutic response is crucial, with predictive factors for response to RLT, such as baseline tumour burden or genetics being discussed. While DNA single- and double-strand breaks have been demonstrated to be early predictors of the efficacy of RLT, germline mutations in DNA-repair genes have been found to have a significantly higher prevalence in patients with mCRPC than in those with localized disease [4]. Furthermore, patients with homologous repair gene mutations have a better therapeutic response to ^{223}Ra therapy [5]. Therefore, studies investigating the clinical effect of DNA-repair gene mutations on the efficacy of ^{177}Lu-PSMA RLT and/or the development of resistance are warranted.

In summary, we report a patient with a diffuse bone marrow carcinomatosis in whom ^{177}Lu-PSMA RLT was highly effective, provided a long-term response and was associated with low toxicity. Thus, such patients should not be excluded from PSMA-targeted RLT, although careful monitoring of organs at risk (e.g. bone marrow) is necessary. Of note, a superscan on bone scintigraphy is an exclusion criterion in the VISION trial (NCT03511664). The significance and risk of serious side effects in diffuse marrow disease has to be explored in further studies, but so far has not been proven to be a clear contraindication to ^{177}Lu-PSMA RLT.

This article is part of the Topical Collection on Image of the Month

✉ Andrei Gafita
andrei.gafita@tum.de

[1] School of Medicine, Department of Nuclear Medicine, Klinikum rechts der Isar, Technical University of Munich, Ismaninger Straße 22, 81675 Munich, Germany

[2] School of Medicine, Department of Urology, Klinikum rechts der Isar, Technical University of Munich, Ismaninger Straße 22, 81675 Munich, Germany

Compliance with ethical standards

Conflict of interest None.

References

1. Hofman MS, Violet J, Hicks RJ, Ferdinandus J, Thang SP, Akhurst T, et al. [(177)Lu]-PSMA-617 radionuclide treatment in patients with metastatic castration-resistant prostate cancer (LuPSMA trial): a single-centre, single-arm, phase 2 study. Lancet Oncol. 2018;19:825–33.
2. Gafita A, Rauscher I, Retz M, Knorr K, Heck M, Wester HJ, et al. Early experience of rechallenge (177)Lu-PSMA radioligand therapy after an initial good response in patients with mCRPC. J Nucl Med. 2019;60:644–8.
3. Gafita A, Bieth M, Kroenke M, et al. qPSMA: a semi-automatic software for whole-body tumor burden assessment in prostate cancer using (68)Ga-PSMA11 PET/CT. J Nucl Med 2019.
4. Pritchard CC, Mateo J, Walsh MF, De Sarkar N, Abida W, Beltran H, et al. Inherited DNA-repair gene mutations in men with metastatic prostate cancer. N Engl J Med. 2016;375:443–53.
5. Isaacsson Velho P, Qazi F, Hassan S, et al. Efficacy of radium-223 in bone-metastatic castration-resistant prostate cancer with and without homologous repair gene defects. Eur Urol. 2018. https://doi.org/10.1016/j.eururo.2018.09.040.