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IMAGE OF THE MONTH

Response to ^{225}Ac-PSMA-I&T after failure of long-term ^{177}Lu-PSMA RLT in mCRPC

Harun Ilhan[1] · Astrid Gosewisch[1] · Guido Böning[1] · Friederike Völter[1] · Mathias Zacherl[1] · Marcus Unterrainer[2] · Peter Bartenstein[1] · Andrei Todica[1] · Franz Josef Gildehaus[1]

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Radioligand therapy (RLT) using ^{177}Lu-PSMA ligands is highly effective in metastatic castration-resistant prostate cancer (mCRPC); however, failure of ^{177}Lu-PSMA RLT remains challenging as RLT already represents last-line treatment.

The α-emitter ^{225}Ac provides higher biological effectiveness compared with ^{177}Lu [1]. Several centers reported remarkable response after PSMA-targeted alpha therapy (TAT) using ^{225}Ac-PSMA-617 after failure of ^{177}Lu-PSMA RLT [2, 3]. Here we present encouraging response to TAT in a patient with advanced mCRPC showing progression after long-term ^{177}Lu-PSMA RLT (10 cycles). PSA values are provided under the date of each PSMA-PET MIP image (A–B using ^{68}Ga-PSMA-11 and E–H using ^{18}F-PSMA-1007). The patient was referred for RLT after radical prostatectomy and radiotherapy in 2005, and anti-hormonal therapy started in 2013 due to biochemical progression. Further progression was observed in February 2017 (A) after 2nd-line anti-hormonal therapy from 2015 to 2016, ^{223}Ra-Dichloride in 2016, and docetaxel chemotherapy from 2016 to 2017. Two cycles of ^{177}Lu-PSMA-617 were highly effective (B). PSA was still decreasing after two additional ^{177}Lu-PSMA-617 cycles despite increasing PSMA-ligand uptake in PSMA-PET (C). Maintenance therapy using ^{177}Lu-PSMA-617 was continued until January 2019 with further response (D and E); however, disease progression occurred after watchful waiting and two cycles of ^{177}Lu-PSMA-I&T (F and G). The patient then received two cycles of ^{225}Ac-PSMA-I&T and showed encouraging response (H). The main TAT-related side effect was grade 2 xerostomia (grade 2), which was already preexisting after 10 cycles of RLT. No TAT-related grade 3/4 hematological side effects were noted. Further cycles are planned but were suspended due to the COVID-19 crisis upon patient's request.

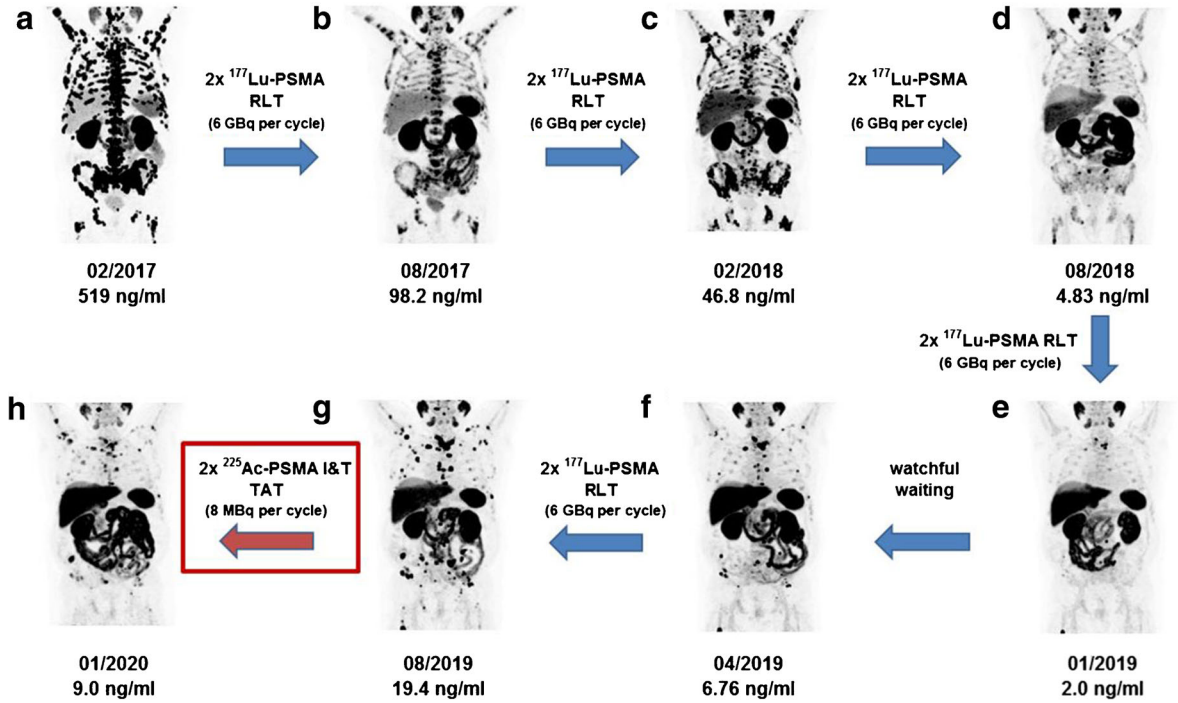
Different approaches including tandem therapy with ^{177}Lu or de-escalating doses during consolidation have been proposed for TAT as a trade-off between therapeutic efficacy and tolerable side effects [2, 4], and further studies investigating ^{225}Ac-PSMA remain highly important for prostate cancer theranostics.

This article is part of the Topical Collection on Image of the month.

✉ Harun Ilhan
harun.ilhan@med.uni-muenchen.de

[1] Department of Nuclear Medicine, University Hospital, LMU Munich, Munich, Germany

[2] Department of Radiology, University Hospital, LMU Munich, Munich, Germany



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Compliance with ethical standards

All procedures performed in this study involving human participants were in accordance with ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This retrospective evaluation was approved by the local ethic committee (20-178). Written informed consent was obtained prior to the exam.

Conflict of interest The authors declare that they have no conflict of interest.

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