Agreement and prediction of response of ^{18}F-rhPSMA-7.3 (Flotufolastat) PET vs. Post-Therapy Scintigraphy to ^{177}Lu-PSMA Radioligand Therapy in APMR Prostate Cancer

Sonia Grigorascu[1 3], Daniel Sasse[1], Isabel Rauscher[1], Robert Tauber[2], Florian Siegel[2], Matthias Eiber[1]
[1]*Department of Nuclear Medicine, TUM-Klinikum Rechts der Isar München, Munich, Germany*
[2]*Department of Urology, TUM-Klinikum Rechts der Isar München, Munich, Germany*
[3]*Contact author, sonia.grigorascu@mri.tum.de*

Introduction and overall goal: Prostate cancer remains the second most common malignancy among US men. Recently, ^{177}Lu-PSMA radioligand therapy (RLT) has emerged as a promising treatment option for patients with Androgen Pathway Modulation-Resistant (APMR) disease.
Specific aims: This retrospective study aimed to analyze pre-therapeutic ^{18}F-flotufolastat (formerly, ^{18}F-rhPSMA-7.3) scans with post-therapeutic scintigraphic ^{177}Lu-PSMA-I&T scans. It compares intermodality agreement of uptake pattern and response to RLT.
Rationale and background: Given the heterogenous benefit of RLT, selecting suitable patients beforehand is crucial. ^{18}F-flotufolastat provides accurate localization of PSMA-positive disease and therefore has potential to assess eligibility for RLT with ^{177}Lu-PSMA-I&T in patients with APMR disease.
Methods and materials: 126 patients with APMR who underwent ^{18}F-flotufolastat PET/CT followed by RLT with ^{177}Lu-PSMA-I&T between 11/2018 and 09/2021 were retrospectively analyzed. PET maximum intensity projection (MIP) and planar anterior and posterior post-therapeutic scintigraphic scans after the first RLT cycle were reviewed by a nuclear medicine resident using a visual scoring scale based on the uptake levels of the majority of lesions: 1=below, 2=equal to, 3=above liver uptake. Comparability between modalities was assessed based on agreement of uptake scores. In addition, PSA progression-free survival (PFS) and PSA response were analyzed, and Kaplan-Meier curves and waterfall plots were generated. All tests and calculations were performed for the entire cohort and after stratification by PET metastatic uptake levels. A P-value <0.05 was considered statistically significant.
Results: A total of 503 cycles of ^{177}Lu-PSMA-I&T (median 4, range 1–10) and a median activity of 7.36 GBq at 1st RLT cycle (range 4.0–9.6) were administered. Eight patients (6.3%), 13 (10.3%), and 105 (83.3%) had a ^{18}F-flotufolastat PET metastatic uptake score of 1, 2, and 3, respectively, compared to 16 (12.7%), 15 (11.9%), and 95 (75.4%) in the planar ^{177}Lu-PSMA-I&T post-therapy scans. Lesion uptake classification (≤liver vs. >liver) showed concordant findings between ^{18}F-flotufolastat PET and post-therapy planar scintigraphy in 80.9% (102/126) of cases, as 14 and 88 patients demonstrated uptake levels ≤liver and >liver on both scans, respectively. PSA values were assessed for 122 patients. The median total PSA-PFS was 3.9 months (95% CI 2.9–4.9), and a >50% PSA response was observed in 39% of patients. Uptake intensity higher than liver uptake on ^{18}F-flotufolastat PET (Group 3) was associated with significantly prolonged PSA-PFS, as patients in this group demonstrated a PSA-PFS of 4.3 months (95% CI 3.4–5.2), compared with 1.6 months (95% CI 0.0–3.8) in PET Groups 1 and 2 (p=0.007). Median PSA response was 59.1% for PET Group 1, 36.3% for PET Group 2, and -17.6% for PET Group 3. A >50% PSA response was achieved in 25.0%, 25.0% and 41.2% for PET Groups 1, 2, and 3, respectively.
Discussion and conclusion: Pre-therapeutic ^{18}F-flotufolastat PET showed lesion uptake scores similar to those on post-therapy ^{177}Lu-PSMA-I&T planar imaging in 80.9% of cases when liver uptake levels were used as the threshold. Moreover, patients with lesions showing high uptake on pre-therapeutic ^{18}F-flotufolastat PET achieved the best PSA response and significantly longer PSA-PFS in our cohort. ^{18}F-flotufolastat is suitable for assessing eligibility for RLT with ^{177}Lu-PSMA-I&T in patients with APMR disease. However, comparability between planar post-therapy ^{177}Lu-PSMA-I&T scans and 3D ^{18}F-flotufolastat scans is limited due to differences in image resolution, as particularly small lesions may not appear on the post-therapy images despite showing high uptake, or may be obscured by organs with physiologically high uptake.