Role of androgen receptor blockade in PSMA expression using ^{68}Ga-PSMA-11 PET/CT imaging in patients with metastatic castrate resistant prostate cancer

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ABSTRACT

Background: ^{68}Ga-PSMA PET/CT plays an important role in the detection and evaluation of metastatic castrate resistant prostate cancer (mCRPC). However, PSMA PET imaging is sensitive to the effects of androgen deprivation therapy (ADT) as several studies have reported a time course effect. Furthermore, there are conflicting findings on whether androgen receptor (AR) blockade in the setting of castrate resistance, enhances lesion detection by ^{68}Ga-PSMA PET/CT. We present preliminary results of a prospective investigator-initiated trial to elucidate the effect of androgen blockade by enzalutamide on the diagnostic sensitivity of ^{68}Ga-PSMA PET/CT.

Methods: mPC patients with demonstrated castrate resistance to standard ADT, rising PSA levels and suitable for standard second-line treatment with an AR blocker, were considered eligible. Patients underwent ^{68}Ga-PSMA-11 PET/CT scans, prepared from an investigational "cold kit" provided by Telix Pharmaceuticals, 28 days prior to enzalutamide treatment and 14-28 days after commencing enzalutamide. PET/CT was quantitatively analysed noting SUV_{max} and SUV_{mean} for each lesion, and total tumour volume. Lesion segmentation was performed using a thresholding method based on the SUV_{mean}+ 2 SD of a 3-cm sphere placed in the right liver lobe on the pre-enzalutamide scan. For one patient with only metastatic lung lesions, a method of 70% thresholding using SUV_{max} was applied as the liver background SUV was higher than SUV of all lung lesions.

Results: To date, 10 patients have been enrolled. Imaging data of one patient who did not complete the post enzalutamide PET/CT was excluded for analysis. For the remaining 9 patients, a median 18% (interquartile range [IQR], -25% - 36%) decrease in total-body SUV_{max} was recorded from pre- to post-enzalutamide scans. PSMA response heterogeneity was noted, with decreasing SUV_{max} in 56% (5/9) of patients and marked increase in 44% (4/9) patients. Similar pattern was recorded for total-body SUV_{mean} with a median 17% ([IQR], -2% - 34%) reduction. Only 11% (1/9) of patients with a high tumour burden showed an increase in SUV_{max}, while 33% (3/9) of patients with a low tumour burden showed an increase in SUV_{max}.

Conclusion: The expression of PSMA post AR blockade as detected by ^{68}Ga-PSMA PET/CT is heterogeneous in this small co-hort. Preliminary results however seem to indicate that in patients with a low tumour burden and predominantly bony metastasis, neoadjuvant enzalutamide could increase the diagnostic sensitivity of ^{68}Ga-PSMA PET/CT.

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