

ORAL PRESENTATION

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PSMA ligands for diagnosis and therapy of prostate cancer

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Since the prostate-specific membrane antigen (PSMA) is frequently over-expressed in prostate cancer (PCa) several PSMA-targeting molecules are under development to detect and treat metastatic castration resistant prostate cancer (mCRPC).

We investigated 319 patients who received a ^{68}Ga -PSMA^{HBED}-PET/CT. In 82.8% of the patients at least one lesion indicative for PCa was detected. Tumor detection was positively associated with PSA level and androgen deprivation therapy (ADT). Mean SUV_{max} of analyzed tumor lesions was 13.3 ± 14.6 . Amongst lesions investigated by histology, 30 were false-negative in ^{68}Ga -PSMA^{HBED}-PET/CT (one local relapse in one patient and 29 lymph nodes in another patient), all other lesions (n=416) were diagnosed true-positive or -negative. Fifty of 116 patients available for follow-up received local therapy after ^{68}Ga -PSMA^{HBED}-PET/CT.

In thirty-seven patients with biochemical relapse of PC a comparison was done between ^{18}F -fluoromethylcholine- and ^{68}Ga -PSMA-PET/CT within a time window of 30 days. Radiotracer uptake that was visually considered as PC lesion was subsequently semi-quantitatively analyzed by measuring the SUV_{max} values of the scans acquired 1 hour p.i. of ^{68}Ga -PSMA complex solution (59 - 263 MBq, median of 132 MBq) and ^{18}F -fluoromethylcholine (114 - 374 MBq, median of 237 MBq) respectively. In addition tumor to background ratios were calculated. 78 PC-suspicious lesions were detected in 32 patients using ^{68}Ga -PSMA-PET/CT and 56 lesions were detected in 26 patients using Choline-PET/CT. The higher detection rate in ^{68}Ga -PSMA-PET/CT concerning PC-suspicious lesions was significant (p=0.04). In 5 patients no lesion was found. All lesions detected by ^{18}F -fluoromethylcholine-PET/CT were also seen by ^{68}Ga -PSMA-PET/CT. In ^{68}Ga -PSMA-PET/CT SUV_{max}

was clearly (>10%) higher in 62 of 78 lesions (79.1%) and tumor-to-background ratio was clearly (>10%) higher in 73 of 78 lesions (93.6%) when compared to ^{18}F -fluoromethylcholine-PET/CT.

Since the ligand bound to PSMA is internalized, the target may also be used for endoradiotherapy. We investigated the tissue kinetics of a small molecule inhibitor of PSMA ((S)-2-(3-((S)-1-carboxy-5-(3-(4-[^{124}I]iodophenyl)ureido)pentyl)ureido)pentanedioic acid; MIP-1095) using PET/CT to estimate radiation dosimetry for the potential therapeutic use of ^{131}I -MIP-1095 in men with mCRPC. We also report preliminary safety and efficacy of the first 28 consecutive patients treated under a compassionate use protocol with a single cycle of ^{131}I -MIP-1095.

I-124-MIP-1095 PET/CT images showed excellent tumor uptake and moderate uptake in liver, proximal intestine and within a few hours post-injection also in the kidneys. High uptake values were observed only in salivary and lacrimal glands. Dosimetry estimates for I-131-MIP-1095 revealed that the highest absorbed doses were delivered to the salivary glands (3.8 mSv/MBq, liver (1.7 mSv/MBq) and kidneys (1.4 mSv/MBq). The absorbed dose calculated for the red marrow was 0.37 mSv/MBq. PSA values decreased by >50% in 60.7% of the men treated. 84.6% of men with bone pain showed complete or moderate reduction in pain. Hematological toxicities were mild. 25% of men treated had a transient slight to moderate dry mouth. No adverse effects on renal function were observed.

Based on the biodistribution and dose calculations of the PSMA-targeted small molecule ^{124}I -MIP-1095 therapy with the authentic analog ^{131}I -MIP-1095 enables a targeted tumor therapy with unprecedented doses delivered to the tumor lesions. Involved lymph node and bone metastases were exposed to estimated absorbed doses upwards of 300 Gy.

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