769 Initial clinical experience with 177Lu-PSMA I&T radionuclide therapy in patients with metastatic castration-resistant prostate cancer

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INTRODUCTION & OBJECTIVES: To report our initial clinical experience with a beta-emitting ^{177}Lutetium-labelled prostate-specific membrane antigen-ligand (^{177}Lu-PSMA I&T) for systemic radionuclide therapy in patients with metastatic castration-resistant prostate cancer (mCRPC).

MATERIAL & METHODS: All patients were treated under a review-board-approved compassionate use protocol. Eligibility criteria for ^{177}Lu-PSMA I&T radionuclide therapy included previous treatment with both chemotherapy and novel androgen-receptor targeted therapy, adequate renal, liver and bone marrow function, Eastern Cooperative Oncology Group (ECOG) performance status ≤1 as well as positive ^{68}Ga-PSMA HBED-CC tracer uptake in metastases in a PET-scan within 4 weeks prior to treatment initiation. Intravenous treatment with ^{177}Lu-PSMA I&T was given 8-weekly in patients with absence of clinical or radiografic progression and absence of severe toxicity (maximum of 4 cycles). To exclude relevant therapy-induced toxicity or side-effects the initial activity was 3.7 GBq in the first cycle of the first 4 patients. Due to low toxicity the activity was increased to 7.4 GBq in the following patients and cycles.

Patients were reevaluated with a ^{68}Ga-PSMA HBED-CC PET-scan after 6 weeks of each cycle and radiographic progression was defined by ≥1 new bone or soft tissue lesion. Clinical symptoms as well as laboratory results including prostate specific antigen (PSA) levels were assessed every 1-2 weeks. Toxicity was evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

RESULTS: 22 patients were eligible to ^{177}Lu-PSMA I&T radionuclide therapy. The number of previous treatment regimens for mCRPC was ≥ 3 in 11 (50%) patients. Bone, lymph node and visceral metastases were present in 20 (91%), 18 (86%) and 10 (45%) patients. At the time of evaluation, the first, second, third and fourth cycle had been initiated in 22, 10, 4 and 4 patients and completed in 17, 9, 4 and 3 patients. The disease control rate (complete remission, partial remission and stable disease) was 65% (11 of 17 patients) after the first cycle, 67% (6 of 9 patients) after the second cycle and 100% after the third (4 of 4 patients) and fourth (3 of 3 patients) cycle. One patient who initially had multiple bone lesions achieved a complete remission after 4 cycles. During the first, second, third and fourth cycle a PSA decline ≥ 30% was achieved in 8 of 17 (47%), 5 of 9 (56%), 3 of 4 (75%) and 1 of 3 (33%) patients. Grade 3/4 toxicities were not observed. The main non-hematologic and hematologic grade 1/2 toxicities were loss of appetite and fatigue in 4 (24%), respectively, dry mouth in 3 (18%) and anemia in 6 (35%) patients.

CONCLUSIONS: ^{177}Lu-PSMA I&T radionuclide therapy appears to be safe and active in late-stage mCRPC. Further evaluation in larger patient cohorts is encouraged.