

Safety and efficacy of Ac-225-PSMA-617 in mCRPC after failure of Lu-177-PSMA

Aim: Despite the approval of several new agents metastatic castration resistant prostate cancer is still a major medical challenge. The beta-emitting Lu-177-PSMA radioligand therapy (RLT) is a new option but its antitumor effect can decrease over time. The aim of this retrospective analysis was to investigate safety and efficacy of the alpha emitting Ac-225-PSMA-617 RLT in mCRPC after Lu-177-PSMA failure.

Methods: 15 patients underwent Ac-225-PSMA-617 RLT between 10/17 and 08/18. All patients had previously received second line antihormonal treatment, as well as chemotherapy and had shown progression after Lu-177-PSMA therapy (median 2 cycles). Repeat PSMA-PET/CT before Ac-225-PSMA-617 therapy indicated continued high PSMA-expression. Patients were treated at 8 weekly intervals until progression or intolerable side effects. Prostate-specific antigen (PSA) and blood cell count were measured every 2-3 weeks. We report hematological and non-hematological side effects (Common Terminology Criteria for Adverse Events) and biochemical response.

Results: A total of 27 cycles of Ac-225-PSMA-617 (median dose 8 MBq, range 6–12.8) were applied. 5 patients received only 1 cycle, 8 patients 2 cycles and 2 patients 3 cycles. Baseline PSA was 758 ng/ml (range 49–4073). ECOG score was grade 0, 1 and 2 in 3, 10 and 2 patients, respectively. 10/15 patients showed any PSA-decline, 5/15 a PSA-decline of more than 50% and 3 patients no PSA-decline at any time. Grade 1-2 xerostomia occurred in 14 and 1 patient, respectively. 5/15 patients requested to stop treatment due to xerostomia. Two patients developed grade 2 renal insufficiency, 4 patients grade 3-4 anemia, 2 patients grade 3 thrombocytopenia. No grade 3-4 leucopenia was observed. 7/15 patients died during the observation period (median overall survival 8 months).

Conclusion: In this small cohort Ac-225-PSMA-617 RLT showed antitumor effect in mCRPC after Lu-177-PSMA failure. However, treatment had to be stopped in one third of the patients due to xerostomia.

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