Ac-225-PSMA617 - a single center experience of 40 patients receiving PSMA-targeted alpha therapy

Abstract:
OBJECTIVES: A case series of 40 patients with advanced stage metastatic castration resistant prostate cancer (mCRPC) treated with alpha-particle emitting Ac-225-PSMA617 was retrospectively evaluated for treatment toxicity and anti-tumor-activity and compared to a similar collective treated with beta-particle emitting Lu-177-PSMA617. METHODS: PSMA-therapy was only offered to patients presenting a PSMA-positive tumor-phenotype on PSMA-PET/CT (Ga-68-PSMA11) or PSMA-SPECT/CT (Tc-99m-MIP1427). Therapy response was evaluated per PSA every 8 weeks and imaging after 24 weeks. Hematologic toxicity was evaluated every 4 weeks per lab tests, clinical side effects were monitored every 8 weeks. Both groups were evaluated for prognostic factors. RESULTS: In regard to Ac-225-PSMA617, 12 patients were treated with varying regimes until a clinical standard procedure (SOP) was defined. From the other 28 patients intended-to-treat (ITT) 20 received therapy and follow-up according to SOP protocol (PP); 3 discontinued due to non-response/progression, 5 due to side-effects. At week-24, i.e. 6 months follow-up, 15/20 (75%) of PP-patients present a PSA-decline, in 11/20 (55%) the PSA-decline was even >80% and correlated with positive imaging response. Hematologic toxicity was not dose limiting even in case of diffuse type red marrow infiltration, but 18/20 patients (90%) reported relevant (substitution needed) xerostomia. In the group treated with Lu-177-PSMA617 only mild moderate xerostomia was reported but hematotoxicity was dose limiting, even if patients with diffuse red-marrow infiltration were excluded. Despite more adverse prognostic factors, response rate was higher for Ac-225- in comparison to Lu-177-PSMA617; but sample size is too small to draw a final conclusion. CONCLUSION: Ac-225-PSMA617 has high activity against mCRPC but xerostomia is a relevant side-effect needing further optimization. The low hematologic toxicity even in presence of diffuse type red-marrow infiltration is remarkable. For patients without red marrow infiltration Lu-177-PSMA617 may be an alternative with less toxicity to salivary glands, but eventually also less anti-tumor-activity.

URI:
http://jnm.snmjournals.org/content/57/supplement_2/1431.abstract [1]

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