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Title: KEYNOTE-046: Effects of ADXS-PSA with or without pembrolizumab on survival and antigen spreading in metastatic, castration-resistant prostate cancer patients
Session: Phase I Clinical Trials: Part 3
Abstract Number: CT098
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Abstract

Background: ADXS-PSA, an attenuated *Listeria monocytogenes*-based immunotherapy targeting prostate-specific antigen (PSA), is currently being evaluated as a treatment for progressive metastatic castration-resistant prostate cancer (mCRPC) in the phase 1/2 KEYNOTE-046 trial as a monotherapy (Part A; PA) and in combination with pembrolizumab (Part B; PB).

Methods: This phase 1/2 trial evaluated pts with mCRPC, ≥18 yrs who received ≤2 prior chemo-/targeted-/immunotherapies or ≤1 prior chemotherapy in a metastatic setting. Part A (PA; n = 13) pts received ADXS-PSA doses $1x10^9$; $5 x10^9$ or $1x10^{10}$ CFU IV every 3 wks and Part B (PB; n = 37) pts received $1x10^9$ CFU + 200 mg pembro IV every 3 wks with a 4^{th} pembro dose 3 wks later (in 12 wks cycles), for up to 2 yrs or until progression/toxicity. Safety/tolerability, antitumor activity and effect on PSA levels have been reported for both groups (Stein M et al., Keynote-046, ASCO 2018). Updates on OS and T cell reactivity to PSA and to other prostate cancer antigens (i.e., prostatic acid phosphatase (PAP), prostate-specific membrane antigen (PSMA), prostate stem cell antigen (PSCA), and prostein) are herein presented for PA and PB pts.

Results: At entry, PA and PB pts were ~70 yrs with a Gleason score >8 and the majority had received prior abiraterone and/or enzalutamide. PB pts had higher median baseline (BL) PSA (40.6 vs. 20.8 ng/mL), and more prior enzalutamide (53 vs. 26%) and chemotherapy (49 vs. 36%) use vs PA pts. Overall, 2 PA (14%) v 16 PB pts (43%) had a decreased PSA post-BL. Of these, 7 PB (19%) vs. 0 PA pts achieved a confirmed PSA reduction ≥50% from BL. The median OS (months) in PB pts was 23.0 (17.4 -NR) vs. 8.5 (3.8-20.10) in PA pts. Median OS in PB pts with PSA reduction ≥50% from BL has not been reached as 100% (6/6) of pts are still alive. T cell reactivity, as measured by ELISpot assays, showed that 100% of PA (9/9) pts and 100% of PB (16/16) pts exhibited increases in the

frequencies of T cells reactive to at least one prostate cancer antigen other than PSA, which is indicative of antigen spreading.

Conclusions: ADXS-PSA **±** pembro elicited a broad antitumor T cell response in all mCRPC pts tested but only ADXS-PSA **+** pembro reduced PSA ≥50% from BL and prolonged OS in these select pts.

Clinical trial information: NCT02325557