61MO Biomarker analysis of men with enzalutamide (enza)-resistant metastatic castration-resistant prostate cancer (mCRPC) treated with pembrolizumab (pembro) + enza in KEYNOTE-199

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Background: In KEYNOTE-199 (NCT02787005), pembrolizumab + enza had durable antitumor activity in enza-refractory mCRPC. We evaluated the association between prespecified biomarkers and clinical outcomes. Methods: Cohorts 4 (C4; RECIST-measurable disease) and 5 (C5; nonmeasurable, bone-predominant disease) enrolled men with chemotherapy-naive mCRPC, irrespective of PD-L1 status, that progressed after initial enza. We evaluated TMB, CPS, and TcellinfGEP in C4 and C5, respectively, achieved a PSA response. TMB was significantly associated with DCR (P < 0.03) and trended toward an association with PSA response (P = 0.08). TMB (AUROC 95% CI: 0.68 (0.51-0.86)), but not CPS (0.54 (0.41-0.67)) or TcellinfGEP (0.35 (0.13-0.74)), enriched for PSA response. TMB (P = 0.04), but not CPS (P = 0.57) or TcellinfGEP (P = 0.32), was significantly associated with PSA progression. There was 1 MSH-p pt (per ProMera PCA assay); this pt achieved an objective and PSA response and had PSF >6 months. TMB, CPS, and TcellinfGEP were not associated with PSF or OS. There was a low prevalence of TMB ≥175 mut/exome (11%) and TcellinfGEP-high (≥ 10316). Conclusions: In this biomarker analysis of KEYNOTE-199 C4-CS, D-LD1 CPS and TcellinfGEP were not significantly associated with clinical outcome. Despite the low prevalence of TMB ≥175 mut/exome, TMB was positively associated with outcomes of pembrolizumab + enza in pts with mCRPC. The sample size for the exploratory analyses were small, and results should be interpreted with caution. Clinical trial identification: NCT02787005. 


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