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Background: In KEYNOTE-199 (NCT02787005), pembro + 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 response to enza. We evaluated TMB by whole exome sequencing (n = 64), PD-L1 combined positive score (CPS) by IHC (n = 124), and 18-gene T-cell–inflamed gene expression profile ($Tcell_{inf}GEP$) by NanoString (n = 51). Outcomes were DCR, PFS, PSA response, PSA progression, OS, and ORR per blinded independent review (C4 only). Significance of continuous biomarkers (CPS, TMB, GEP) was prespecified at 0.05 for 1-sided *P* values from logistic (ORR, DCR, PSA response) and Cox proportional hazard (PFS, OS, PSA progression) regression adjusted for ECOG PS.

Results: In C4, ORR was 10% (5/48) in pts with evaluable TMB data and 12% (10/81) in pts with CPS data. In C4 and C5, 16% (10/64) and 14% (17/124) of pts with TMB and CPS data, 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 $Tcell_{inf}GEP$ (0.55 [0.37-0.74]), enriched for PSA response. TMB ($P = 0.04$), but not CPS ($P = 0.57$) or $Tcell_{inf}GEP$ ($P = 0.32$), was significantly associated with PSA progression. There was 1 MSI-H pt (per Promega PCR assay); this pt achieved an objective and PSA response and had PFS >6 months. TMB, CPS, and $Tcell_{inf}GEP$ were not associated with PFS or OS. There was a low prevalence of TMB ≥175 mut/exome (11%) and $Tcell_{inf}GEP$-high (≥−0.318; 16%).

Conclusions: In this biomarker analysis of KEYNOTE-199 C4-C5, PD-L1 CPS and $Tcell_{inf}GEP$ were not significantly associated with clinical outcome. Despite the low prevalence of TMB ≥175 mut/exome, TMB was positively associated with outcomes of pembro + enza in pts with mCRPC. The sample sizes for the exploratory analyses were small, and results should be interpreted with caution.

Clinical trial identification: NCT02787005.

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62P Markers in assessment of osteoporosis therapy efficiency in hormone-dependent breast cancer

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Background: Our purpose was to evaluate bone remodeling markers in assessing the efficiency of osteoporosis therapy in hormone-dependent breast cancer (BC).

Methods: The study included 102 patients: 60.0±5.0 years, in menopause for 5 years, luminal BC after mastectomy, receiving adjuvant hormonal therapy with aromatase inhibitors and osteoporosis therapy with denosumab (120 mg subcutaneously) or zoledronic acid (4 mg intravenously) every 6 months. The groups were: 1A (n=24) with luminal A and 1B (n=28) with luminal B subtypes receiving denosumab; 2A (n=26) with luminal A and 2B (n=24) with luminal B subtypes receiving zoledronic acid. The bone tissue status was assessed by bone scintigraphy and osteodensitometry. P1NP, β-Cross laps, and osteocalcin were studied before and after 6, 12, 18, and 24 months of osteoporosis therapy.

Results: Before the treatment, osteoporosis was found in group 1A - 15 patients, 1B - 13, 2A – 16, 2B – 17. An increase in the bone mineral density in comparison with the initial values was observed in groups 1A and 1B during treatment, unlike groups 2A and 2B. Initial levels of β-Cross laps in all patients were 1.020±0.009 ng/ml (vs. normal levels 1.009 ng/ml); in 24 months, their decrease was noted, more pronounced in groups 1B (0.882±0.024 ng/ml, $p<0.01$) and 2B (0.816±0.037, $p<0.001$), indicating reduced intensity of pathological bone resorption. Initial P1NP levels were within the reference range in all patients (16.27-73.87 mcg/l). In 24 months, P1NP increased in groups 1B and 2B, indicating the activation of osteosynthesis processes. Initial osteocalcin levels were increased (vs. the norm - 46 ng/ml) in all patients, with the maximum values in groups 1A (62.36±6.30 ng/ml) and 2A (61.65±6.10 ng/ml), which indicated bone metabolism suppression. The values decreased during the treatment, especially in groups 1A (40.93±4.30 ng/ml) and 1B (45.09±4.4 ng/ml), compared to initial levels ($p<0.05$). Patients in groups 2A and 2B did not show statistically significant changes in osteocalcin levels.

Conclusions: P1NP, β-Cross laps, and osteocalcin values are promising in monitoring the efficiency of osteoporosis therapy in BC patients. Denosumab is more effective in preventing pathological bone resorption.

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