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TUMOR MUTATIONAL BURDEN (TMB) IS A POTENTIAL PREDICTOR OF RESPONSE TO IMMUNE CHECKPOINT INHIBITORS (ICI) IN METASTATIC TRIPLE-NEGATIVE BREAST CANCER (MTNBC)

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Objectives: This study aimed to explore if TMB correlates with efficacy of PD-1/PD-L1 inhibition in patients (pts) with mTNBC. **Methodology**: Demographic, treatment response, and long-term outcome data were collected on patients with mTNBC treated at Dana-Farber Cancer Institute (DFCI) under several clinical trials incorporating PD-1/PD-L1 inhibitors, given as monotherapy or combined with chemotherapy (CT). Pts included in this analysis had available results of targeted exon sequencing performed using Oncopanel, our institutional gene sequencing panel, on archival tumor tissue. TMB was calculated by determining the number of non-synonymous somatic mutations that occur per megabase of exonic sequence data across all genes on the panel. High TMB was defined as 10 mutations/megabase. TMB and gene alterations were correlated with objective response rate (ORR) per RECIST 1.1, progression-free (PFS) and overall survival (OS). **Results:** A total of 48 pts with mTNBC were included in this analysis. At baseline, the median age was 55.9 years (31.8–75.9), 60% had ECOG 0 and 40% had ECOG 1, 72% had visceral metastasis, and 46% had received >1 prior lines of systemic therapy in the metastatic setting. While 26% of pts received monotherapy [pembrolizumab (n=7, NCT02447003); atezolizumab (n=6; NCT01375842)], 74% received combination with CT [pembrolizumab plus eribulin (n=31; NCT02513472); atezolizumab plus nab-paclitaxel (n=6; NCT01633970)]. Median follow-up was 14 months (1–40). The median TMB was 6.6 mut/Mb (1.2–50.8), and 23% of pts had a high TMB. While high TMB was not associated with higher ORR (p=0.56), it was associated with better median PFS (16.5 vs 2.4 months; p=0.017), and better median OS (not reached vs 13.5 months; p=0.026). TMB remained significantly associated with PFS in the multivariable model. **Conclusion:** High TMB may impact benefit from PD-1/PD-L1 inhibitors largely administered with chemotherapy in mTNBC. This observation warrants prospective validation.