THREE-YEAR OUTCOMES WITH FIRST-LINE PEMBROLIZUMAB FOR METASTATIC NON–SMALL-CELL LUNG CANCER (NSCLC) WITH A VERY HIGH PD-L1 TUMOR PROPORTION SCORE (TPS) ≥ 90%

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Background Although 1st-line PD-1 monotherapy has improved survival in patients with advanced NSCLC and a PD-L1 TPS ≥50%, responses occur in ~45% of patients. We have previously shown that among patients with NSCLC and PD-L1 expression of ≥50% treated with 1st-line pembrolizumab, clinical outcomes are significantly improved in those with a PD-L1 TPS of ≥90%. Here, we report the 3-year follow-up outcomes to 1st-line pembrolizumab in patients with a PD-L1 TPS ≥90% vs <50–89%, and genomic differences between these groups.

Methods Patients with stage IV EGFR/ALK wild type NSCLC and PD-L1 TPS ≥50% who received 1st-line pembrolizumab monotherapy at Dana-Farber Cancer Institute were included. Comprehensive tumor genomic profiling was performed to examine genomic correlates of a very high PD-L1 expression on an expanded cohort of NSCLC samples.

Results Among 150 patients included, median age was 69 (range: 46–92), 55.3% were women, 91.9% were current smokers, and 34.0% had a KRAS mutation. At a median follow-up of 38.5 months, median progression-free (mPFS) and overall survival (mOS) in the entire cohort were 4.8 months, and 20.0 months, respectively. When compared to patients with a PD-L1 expression of 50–89% (N=81), those with PD-L1 TPS ≥90% (N=69) had a significantly longer mPFS (6.0 vs 3.9 months, HR 0.66, P=0.02), and longer mOS (27.0 vs 14.6 months, HR 0.63, P=0.03; figure 1). Kaplan-Meier estimates of the 3-year PFS and OS were 23.0% and 43.2% in the PD-L1 TPS ≥90% groups, and 8.6% and 24.0% in the PD-L1 TPS 50–89% group, respectively. A PD-L1 TPS ≥90% was confirmed to be an independent predictor of improved PFS (HR 0.58, P=0.02) and OS (HR 0.57, P=0.01) at multivariable analysis. Patients whose tumors had a PD-L1 TPS ≥90% were also significantly more likely to complete 35 cycles of therapy compared to those with PD-L1 TPS of 50–89% (17.4% vs 3.7%, P<0.01, figure 2). Tumor genomic profiling from 500 NSCLC samples revealed that mutations in STK11, KEAP1, FBXW7, and CTNNB1, which have been previously correlated with immunotherapy resistance, were significantly enriched tumors with a PD-L1 TPS of 50–89% compared to those with a PD-L1 TPS ≥90% (figure 3).

Conclusions Pembrolizumab monotherapy continues to demonstrate a meaningful long-term survival benefit at a 3-year follow-up in patients with advanced NSCLC and a PD-L1 TPS ≥90% vs 50–89%. NSCLCs with very high PD-L1 TPS have a more favorable genomic profile. These findings have implications for treatment selection and for clinical trial interpretation and design.

REFERENCE


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