Background Primary analysis of KEYNOTE-042 (NCT02220894), a global, randomized, phase 3 trial, showed that pembrolizumab significantly improved OS versus platinum-based chemotherapy in patients with locally advanced or metastatic non–small-cell lung cancer (NSCLC) without sensitizing EGFR/ALK alterations and with PD-L1 tumor proportion score (TPS) $\geq 50\%$, $\geq 20\%$, and $\geq 1\%$ with fewer treatment-related AEs than chemotherapy. We report an updated analysis with ~5 years of follow-up.

Methods Eligible adults were randomized 1:1 to receive pembrolizumab 200 mg Q3W for 35 cycles or investigator choice of chemotherapy (carboplatin + paclitaxel or pemetrexed) Q3W for 6 cycles with optional maintenance pemetrexed (nonsquamous only). Primary endpoints were OS and PFS and ORR per RECIST v1.1 by central review, and safety (secondary). Eligible patients randomized to pembrolizumab who completed 35 cycles with SD or better or ORR were included in the updated analysis. OS was estimated with the Kaplan-Meier method; PFS and ORR were summarized with the rates per RECIST v1.1.

Results 1274 patients were randomized to pembrolizumab or chemotherapy (n = 637 each). Median (range) time from randomization to data cutoff (Apr 28, 2021) was 61.1 (50.0–76.3) months. OS outcomes favored the pembrolizumab group (vs chemotherapy alone) regardless of PD-L1 TPS (HR [95% CI] for TPS $\geq 50\%$, 0.68 [0.57–0.81]; TPS $\geq 20\%$, 0.75 [0.64–0.87]; TPS $\geq 1\%$, 0.79 [0.70–0.89]), with estimated 5-year OS rates (95% CI) of 21.9% (17.3%–26.9%), 19.4% (15.6%–23.4%), and 16.6% (13.7%–19.6%), respectively, in the pembrolizumab group (table 1).

Conclusions With 5 years of follow-up, first-line pembrolizumab monotherapy continued to show substantial clinical benefit with higher 5-year OS rates, and durable response over chemotherapy in patients with PD-L1–positive, locally advanced/metastatic NSCLC without EGRF/ALK alterations. First-line pembrolizumab remains a standard of care in patients with PD-L1 TPS $\geq 1\%$, as underscored by these long-term results.

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