363 KEYNOTE-042 5-YEAR SURVIVAL UPDATE: PEMBROLIZUMAB VERSUS CHEMOTHERAPY IN PATIENTS WITH PREVIOUSLY UNTREATED, PD-L1–POSITIVE, LOCALLY ADVANCED OR METASTATIC NON–SMALL-CELL LUNG CANCER

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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) ≥50%, ≥20%, and ≥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's choice of chemotherapy (carboplatin + paclitaxel or pemetrexed) Q3W for 4–6 cycles with optional maintenance pemetrexed (nonsquamous only). Primary endpoints were OS in patients with PD-L1 TPS ≥50%, ≥20%, and ≥1%; secondary endpoints included 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 stopped treatment after confirmed CR could begin a second course of pembrolizumab at the time of progression.

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 ≥50%, 0.68 [0.57–0.81]; TPS ≥20%, 0.75 [0.64–0.87]; TPS ≥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**). Median duration of response (DOR) was 28.1 vs 10.8 months in PD-L1 TPS ≥50% group, 27.7 vs 10.8 months in PD-L1 TPS ≥20% group and, 26.5 vs 8.4 months in PD-L1 TPS ≥1% for pembrolizumab group vs chemotherapy. Treatment-related grade 3–5 AEs occurred in 120 patients (18.9%) in the pembrolizumab group and 257 (41.8%) in the chemotherapy group. Among 102 patients who completed 35 cycles of pembrolizumab: ORR was 84.3%; estimated 4-year OS rate after completion of 35 cycles of pembrolizumab (ie, approximately 6 years after randomization) was 61.8%. Among 33 patients who received second-course pembrolizumab, ORR was 15.2%.

Abstract 363 Table 1 Key efficacy outcomes in the KEYNOTE-042 ITT population

ITT Population	PD-L1 TPS ≥50%		PD-L1 TPS ≥20%		PD-L1 TPS ≥1%	
	Pembrolizumab n = 299	Chemo n = 300	Pembrolizumab n = 413	Chemo n = 405	Pembrolizumab n = 637	Chemo n = 637
OS, median (95% CI), mo	20.0 (15.9–24.2)	12.2 (10.4–14.6)	18.0 (15.5–21.5)	13.0 (11.6–15.3)	16.4 (14.0–19.6)	12.1 (11.3–13.3)
OS, HR (95% CI)	0.68 (0.57–0.81)		0.75 (0.64–0.87)		0.79 (0.70–0.89)	
OS, 5 y rate (95% CI), %	21.9 (17.3–26.9)	9.8 (6.6–13.7)	19.4 (15.6–23.4)	10.1 (7.2–13.5)	16.6 (13.7–19.6)	8.5 (6.4–11.0)
PFS, median (95% CI), mo	6.5 (5.9–8.6)	6.5 (6.2–7.6)	6.2 (5.4–7.8)	6.9 (6.3–8.2)	5.6 (4.3–6.2)	6.8 (6.4–7.9)
PFS, HR (95% CI)	0.86 (0.72–1.02)		0.94 (0.81–1.09)		1.03 (0.91–1.16)	
PFS, 5 y rate (95% CI), %	9.2 (5.9–13.4)	2.1 (0.7–5.0)	7.8 (5.2–11.1)	1.6 (0.5–3.9)	6.9 (4.9–9.4)	1.2 (0.5–2.7)
PFS2[a], median (95% CI), mo	15.0 (11.6–19.2)	10.1 (8.9–11.2)	12.9 (10.9–15.5)	10.2 (9.1– 11.3)	11.3 (10.1–12.9)	9.4 (8.8–10.3)
PFS2[a], HR (95% CI)	0.64 (0.54–0.76)		0.67 (0.58–0.78)		0.74 (0.65–0.83)	
ORR (95% CI), %	39.1 (33.6–44.9)	32.3 (27.1–37.9)	33.2 (28.6–37.9)	29.1 (24.8–33.8)	27.3 (23.9–31.0)	26.7 (23.3–30.3)
DOR, median (range), mo	28.1 (2.1+ to 70.0+)	10.8 (1.8+ to 63.5+)	27.7 (2.1+ to 70.0+)	10.8 (1.8+ to 63.5+)	26.5 (2.1+ to 70.0+)	8.4 (1.8+ to 63.5+)

Chemo, chemotherapy; DOR, duration of response.
+, indicates no PD by the time of last assessment.
[a]PFS2: time from randomization to second/subsequent PD on next-line treatment or death.

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 *EGFR/ALK* alterations. First-line pembrolizumab remains a standard of care in patients with PD-L1 TPS ≥1%, as underscored by these long-term results.

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Trial Registration ClinicalTrials.gov, NCT02220894

Ethics Approval The protocol and all amendments were approved by the appropriate ethics committee at each center, the study was conducted in accordance with the Standards of Good Clinical Practice and in compliance with the Declaration of Helsinki. Patients provided written informed consent before enrollment.

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