NSCLC, early stage

LBA56 Overall survival in the KEYNOTE-671 study of perioperative pembrolizumab for early-stage non-small-cell lung cancer (NSCLC)

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Background: At the protocol-specified first interim analysis of the phase 3 KEYNOTE-671 study of resectable early-stage NSCLC (NCT03425643), neoadjuvant pembrolizumab (pembro) + chemotherapy (chemo) followed by resection and adjuvant pembro significantly improved EFS, mPR, and pCR with an expected safety profile vs neoadjuvant chemo and resection alone. We present results of the protocol-specified second interim analysis of KEYNOTE-671.

Methods: Patients (pts) with resectable stage II, IIIA, or IIIB (N2) NSCLC per AJCC v8 were randomized 1:1 to pembro 200 mg (n = 397) or placebo (n = 400) Q3W. Pts were to receive 4 cycles of neoadjuvant pembro or placebo plus cisplatin-based chemo and ≤13 cycles of adjuvant pembro or placebo. Dual primary endpoints are EFS (time from randomization to local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause) and OS.

Results: Median time from randomization to the 10 July 2023 data cutoff was 36.6 mo (range, 18.8-62.0). With 254 (31.9%) deaths, OS was significantly improved in the pembro arm (HR 0.72 [95% CI 0.56-0.93]; $P = 0.00517$). Median OS was not reached (NR) (95% CI NR-NR) in the pembro arm vs 52.4 mo (95% CI 45.7-NR) in the placebo arm; 36-mo OS rates were 71.3% vs 64.0%. EFS continued to be improved in the pembro arm (HR 0.59 [95% CI 0.48-0.72]; median [95% CI] 47.2 mo [32.9-NR] vs 18.3 mo [14.8-22.1]; 36-mo rate, 54.3% vs 35.4%). Treatment-related AEs were grade ≥3 in 45.2% of pts in the pembro arm vs 37.8% in the placebo arm, led to discontinuation of all treatment in 20.2% vs 9.3%, and led to death in 1.0% vs 0.8% (no new treatment-related deaths since the first interim analysis).

Conclusions: Neoadjuvant pembro + chemo followed by resection and adjuvant pembro provided a statistically significant and clinically important improvement in OS compared with neoadjuvant chemo and resection alone in pts with resectable stage II, IIIA, or IIIB (N2) NSCLC. The OS gains seen in KEYNOTE-671 with the absence of new safety signals establish the perioperative pembro regimen as a new standard of care for resectable early-stage NSCLC.

Clinical trial identification: NCT03425643, first posted February 7, 2018.

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LBA57 Neoadjuvant nivolumab (N) + chemotherapy (C) in the phase III CheckMate 816 study: 3-y results by tumor PD-L1 expression

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Background: In CheckMate 816, neoadjuvant N + C vs C significantly improved the primary endpoints of event-free survival (EFS) and pathological complete response (pCR) in patients with resectable NSCLC; 3-y EFS benefit with N + C vs C was also demonstrated. Here, we report clinical outcomes by baseline tumor PD-L1 expression.

Methods: Adults with stage IB ($\geq$ 4 cm)—IIIA (AJCC v7) resectable NSCLC were randomized 1:1 to receive N 360 mg + C Q3W or C Q3W for 3 cycles. Exploratory analyses included EFS, overall survival (OS), pCR, major pathological response (MPR), surgical outcomes, and safety in patients with tumor PD-L1 $\geq$ 1% or $<$ 1%.

Results: In patients with tumor PD-L1 $\geq$ 1% (N + C, 89; C, 89) and PD-L1 $<$ 1% (78; 77), baseline characteristics were generally similar between PD-L1 subgroups and treatment arms. A higher proportion of patients with tumor PD-L1 $<$ 1% had ECOG PS 1 (both arms). At database lock (14 Oct 2022; median follow-up, 41.4 mo), N + C showed improvement vs C across all efficacy endpoints in patients with tumor PD-L1 $\geq$ 1% (Table); 3-y EFS and OS rates were 72% vs 47% and 85% vs 66%, respectively. Similar efficacy benefit was seen in patients with tumor PD-L1 $\geq$ 1% and stage II—IIIA NSCLC (data to be presented). In patients with tumor PD-L1 $<$ 1%, EFS, OS, pCR, and MPR also favored N + C vs C (Table); 3-y EFS and OS rates were 42% vs 39% and 71% vs 60%, respectively. Definitive surgery rates with N + C vs C were 84% vs 74% in patients with tumor PD-L1 $\geq$ 1% and 81% vs 77% in patients with tumor PD-L1 $<$ 1%; R0 resection rates were 91% vs 82% and 79% vs 76%, respectively. Grade 3—4 treatment-related AE rates with N + C vs C were 34% vs 44% in patients with tumor PD-L1 $\geq$ 1% and 36% vs 34% in patients with tumor PD-L1 $<$ 1%.

Conclusions: These exploratory analyses from CheckMate 816 reinforce the clinical benefit and manageable safety profile of neoadjuvant N + C in patients with resectable NSCLC regardless of tumor PD-L1 expression.

Clinical trial identification: NCT02998528.

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Table: LBA57 Efficacy outcomes by tumor PD-L1 expression

	Tumor PD-L1 ≥ 1%		Tumor PD-L1 < 1%	
	N + C (n = 89)	C (n = 89)	N + C (n = 78)	C (n = 77)
EFS				
Median, mo (95% CI)	NR (44.4—NR)	26.7 (13.4—NR)	26.4 (14.8—NR)	20.8 (13.9—42.1)
HR (95% CI)	0.46 (0.28—0.77)		0.87 (0.57—1.35)	
OS				
Median, mo (95% CI)	NR (NR—NR)	NR (45.1—NR)	NR (48.6—NR)	NR (31.2—NR)
HR (95% CI)	0.37 (0.20—0.71)		0.81 (0.48—1.36)	
pCR rate, % (95% CI)	32.6 (23.0—43.3)	2.2 (0.3—7.9)	16.7 (9.2—26.8)	2.6 (0.3—9.1)
MPR rate, % (95% CI)	44.9 (34.4—55.9)	5.6 (1.8—12.6)	29.5 (19.7—40.9)	14.3 (7.4—24.1)

NR, not reached.