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Perioperative pembrolizumab in early-stage non-small-cell lung cancer (NSCLC): 5-year follow-up from KEYNOTE- 671

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Background

In the global, phase 3 KEYNOTE-671 study (NCT03425643), perioperative pembrolizumab (pembro) significantly improved event-free survival (EFS; HR, 0.58; 95% CI, 0.46–0.72; $P < 0.001$) and OS (IA2; HR, 0.72; 95% CI, 0.56–0.93; $P = 0.0052$) vs neoadjuvant chemotherapy (chemo) in early-stage NSCLC. We report results after 5 years of follow-up from KEYNOTE-671.

Methods

Eligible participants (pts) aged ≥ 18 years with previously untreated, resectable stage II, IIIA, or IIIB (N2) NSCLC per AJCC version 8 were randomized 1:1 to 4 cycles of pembro 200 mg or placebo Q3W plus chemo, followed by surgery then adjuvant pembro 200 mg or placebo Q3W for up to 13 cycles (~9 months) or until PD or unacceptable toxicity. Dual primary endpoints were EFS per RECIST version 1.1 by investigator assessment and OS.

Results

797 pts were randomized to pembro ($n = 397$) or placebo ($n = 400$). Median time from randomization to data cutoff (July 3, 2025) was 60.4 (range, 42.6–85.8) months. The 5-year EFS rate was 49.9% (95% CI, 44.6%–55.0%) in the pembro arm and 26.5% (95% CI, 21.7%–31.5%) in the placebo arm; EFS HR was 0.58 (95% CI, 0.48–0.69). 5-year OS rates were 64.6% (95% CI, 59.5%–69.2%) and 53.6% (95% CI, 48.3%–58.6%), respectively; OS HR was 0.74 (95% CI, 0.59–0.92). HRs for EFS and OS favored pembro regardless of baseline disease stage and PD-L1 status (Table). Grade ≥ 3 treatment-related AEs occurred in 179 of 396 treated pts (45.2%) in the pembro arm and 151 of 399 treated pts (37.8%) in the placebo arm. Grade ≥ 3 immune-mediated AEs and infusion reactions occurred in 25 pts (6.3%) and 7 pts (1.8%), respectively. Table: LBA67

	Pembro arm (n = 397)	Placebo arm (n = 400)
EFS ^a		
Median (95% CI), mo	57.1 (38.0–NR)	18.4 (14.8–22.1)
5-y rate (95% CI)	49.9 (44.6–55.0)	26.5 (21.7–31.5)
HR (95% CI)	0.58 (0.48–0.69)	
OS		

	Pembro arm (n = 397)	Placebo arm (n = 400)
Median (95% CI), mo NR (NR–NR)		70.7 (53.7–NR)
5-y rate (95% CI)	64.6 (59.5–69.2)	53.6 (48.3–58.6)
HR (95% CI)	10.74 (0.59–0.92)	
	EFS ^a HR (95% CI)	OS HR (95% CI)
Stage ^b		
II (n = 239)	0.52 (0.35–0.76)	0.67 (0.43–1.05)
III (n = 558)	0.58 (0.47–0.72)	0.75 (0.58–0.96)
PD-L1 TPS ^b		
≥50% (n = 266)	0.44 (0.31–0.64)	0.65 (0.42–1.00)
1%–49% (n = 242)	0.54 (0.39–0.75)	0.67 (0.45–0.99)
<1% (n = 289)	0.74 (0.55–0.98)	0.87 (0.62–1.21)

NR, not reached; TPS, tumor proportion score. ^aPer investigator assessment. ^bAt baseline.

Conclusions

After 5 years of follow-up, perioperative pembro plus neoadjuvant chemo continued to prolong EFS and OS vs neoadjuvant chemo. Fifty percent of pts in the pembro arm, almost twice as many as in the placebo arm, were alive and event-free at 5 years. These long-term findings support use of perioperative pembro plus neoadjuvant chemo as a standard of care for patients with resectable early-stage NSCLC.

Clinical trial identification

NCT03425643; EU CT, 2017-001832-21.

Editorial acknowledgement

Medical writing assistance was provided by Aisling Towell, PhD, of ICON plc (Blue Bell, PA, USA). This assistance was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Legal entity responsible for the study

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Funding

Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Disclosure

H. Wakelee: Financial Interests, Personal, Invited Speaker, Develop and present a series of lectures: Fishawack Facilitate LTD; Financial Interests, Personal, Invited Speaker, Series of CME lectures: Medscape, Research to Practice; Financial Interests, Personal, Other, Discussion of new data at conferences: Curio Science; Financial Interests, Personal, Invited Speaker, Series of lectures/webinars for PER/OncLive: MJH Holdings; Financial Interests, Personal, Advisory Board: IOBiotech, GSK; Financial Interests, Personal, Invited Speaker, Facilitated speaking at several virtual conferences: Shanghai Bird Translation and Consulting; Financial Interests, Personal, Invited Speaker, Invited to speak and moderate at JLCS meetings: Japanese Lung Cancer Society; Financial Interests, Personal, Invited Speaker, Presented at several CME conferences: Medical Educator Consortium; Financial Interests, Personal, Invited Speaker, Facilitated discussion of recent data: IDEOlogy Health; Financial Interests, Personal, Invited Speaker, Invited CME lecture: Vindico Medical Education; Financial Interests, Personal, Invited Speaker, CME lecture: ParadigmMC, Prova Education; Financial Interests, Personal, Invited Speaker, Invited speaker at symposium: Taiwan Association for the Study of Lung Cancer (TASLC); Financial Interests, Personal, Advisory Board, Part of Scientific Advisory Board: OncoC4; Financial Interests, Personal, Invited Speaker, Travel and honorarium paid for CME lectures: Chugai Pharmaceutical; Financial Interests, Personal, Advisory Board, Served on Advisory Board: BeiGene; Financial Interests, Personal, Royalties, I receive royalties for a chapter I wrote for UpToDate: UpToDate; Financial Interests, Institutional, Local PI, Clinical Trial Conduct: AstraZeneca/Medimmune, BMS, Seagen, Xcovery; Financial Interests, Institutional, Steering Committee Member, Clinical Trial Conduct: Genentech/Roche, Merck; Financial Interests, Institutional, Local PI, clinical trial conduct: Helsinn; Financial Interests, Institutional, Coordinating PI, IIT for single site: Bayer; Financial Interests, Personal, Steering Committee Member, uncompensated steering committee member: Merck, AstraZeneca, Genentech/Roche; Financial Interests, Personal, Other, uncompensated advisory board participation: BMS; Financial Interests, Institutional, Local PI, Local PI for IIT coordinated by another institution but with trial support from Gilead to the other institution.: Gilead; Non-Financial Interests, Officer, Past President: International Association for the Study of Lung Cancer (IASLC); Non-Financial Interests, Leadership Role, Executive Committee: ECOG-ACRIN. J. Spicer: Financial Interests, Institutional, Research Grant:

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