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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
Disclosure

All other authors have declared no conflicts of interest.

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