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Amivantamab plus chemotherapy vs chemotherapy as first-line treatment in EGFR Exon 20 insertion-mutated advanced non-small cell lung cancer (NSCLC): Primary results from PAPILLON, a randomized phase III global study


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Background
Amivantamab (ami) is an EGFR-MET bispecific antibody with immune cell–directing activity. Ami combined with carboplatin/pemetrexed (ami-chemo) demonstrated safety and antitumor activity in the phase 1 CHRYSALIS study. PAPILLON (NCT04538664) evaluated ami-chemo vs chemo in first-line EGFR Ex20ins advanced NSCLC.

Methods
Treatment-naïve pts were randomized 1:1 to ami-chemo or chemo. The primary endpoint was progression-free survival (PFS) by blinded independent central review. Secondary endpoints included objective response rate (ORR), PFS after first subsequent therapy (PFS2), overall survival (OS), and safety. Crossover to ami monotherapy was allowed for the chemo arm upon progression.

Results
Overall, 308 pts were randomized (ami-chemo, 153; chemo, 155); median age was 61/62 years, 56/60% female, 64/59% Asian, and 23/23% with history of brain metastases for ami-chemo/chemo, respectively. At median follow-up of 14.9 months, the median PFS was 11.4 months (95% CI, 9.8–13.7) for ami-chemo vs 6.7 months (95% CI, 5.6–7.3) for chemo (hazard ratio [HR], 0.40; 95% CI, 0.30–0.53; P<0.001). The 18-month PFS rate was 31% for ami-chemo vs 3% for chemo. PFS benefit of ami-chemo was consistent across subgroups. ORR was 73% (95% CI, 65–80) for ami-chemo vs 47% (95% CI, 39–56) for chemo (odds ratio, 2.97; 95% CI, 1.84–4.79; P<0.001). Median PFS2 was not estimable for ami-chemo vs 17.2 months for chemo (HR, 0.49; 95% CI, 0.32–0.76; P=0.001). Interim OS analysis (33% maturity) showed a favorable trend for ami-chemo vs chemo (HR, 0.67; 95% CI, 0.42–1.09; P=0.106), despite 66%, of chemo-randomized pts whose disease had progressed, receiving second-line ami. The most common TEAEs (≥40%) for ami-chemo were neutropenia, paronychia, rash, anemia, infusion-related reactions, and hypoalbuminemia; no new safety signals. Discontinuation of ami due to treatment-related AEs was 7%.

Conclusions
Among pts with EGFR Ex20ins advanced NSCLC, ami-chemo achieved superior PFS vs chemo. Safety profile was consistent with that of each individual agent. PAPILLON establishes ami-chemo as the new first-line standard of care in EGFR Ex20ins advanced NSCLC.

Clinical trial identification
NCT04538664.

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