Amivantamab plus lazertinib vs osimertinib as first-line treatment in patients with EGFR-mutated, advanced non-small cell lung cancer (NSCLC): Primary results from MARIPOSA, a phase III, global, randomized, controlled trial


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Background
Amivantamab (ami), an EGFR-MET bispecific antibody with immune cell-directing activity, plus lazertinib (laz), a CNS-penetrant, 3rd-generation EGFR TKI, have demonstrated antitumor activity in phase 1 studies. MARIPOSA (NCT04487080) evaluated ami+laz vs osimertinib (osi) in the first-line setting.

Methods
Patients (pts) with treatment-naive, EGFR-mutated (Ex19del or L858R) locally advanced or metastatic NSCLC were randomized 2:2:1 to ami+laz, osi, or laz. Primary endpoint was progression-free survival (PFS) of ami+laz vs osi by blinded independent central review. Secondary endpoints included overall survival (OS), objective response rate (ORR), duration of response (DoR), PFS after first subsequent therapy (PFS2), and safety. CNS monitoring was required.

Results
1074 pts were randomized (ami+laz, 429; osi, 429; laz, 216). Baseline characteristics were balanced; median age was 63 years, 62% were female, 59% Asian, and 41% had a history of brain metastases. At a median follow-up of 22.0 months (mo), ami+laz showed a 30% reduction in the risk for disease progression or death vs osi (HR, 0.70; 95% CI, 0.58–0.85; P<0.001), with median PFS of 23.7 mo (95% CI, 19.1–27.7) vs 16.6 mo (95% CI, 14.8–18.5), respectively. ORR was 86% (95% CI, 83–89) for ami+laz vs 85% (95% CI, 81–88) for osi, with median DoR among confirmed responders of 25.8 mo (95% CI, 20.1–NE) vs 16.8 mo (95% CI, 14.8–18.5), respectively. Early PFS2 data favored ami+laz vs osi (HR, 0.75; 95% CI, 0.58–0.98). At interim OS, there was a favorable trend for ami+laz over osi (HR, 0.80; 95% CI, 0.61 to 1.05; P=0.1). EGFR- and MET-related AEs were higher for ami+laz except diarrhea, which was higher for osi. VTEs were increased for ami+laz, mostly grade 1-2, occurred early, and effectively managed with anticoagulants.ILD rates were low and similar across arms.

Conclusions
Ami+laz was statistically superior to osi, providing clinically meaningful improvement in PFS, with higher DoR and a favorable OS trend. The safety profile of ami+laz was consistent with prior reports. MARIPOSA establishes ami+laz as a new first-line, standard of care for EGFR-mutated advanced NSCLC.

Clinical trial identification
NCT04487080.

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Legal entity responsible for the study
Janssen Global Services LLC.
Disclosure


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