

Amivantamab Plus Lazertinib vs Osimertinib in First-line EGFR-mutant Advanced NSCLC: Longer Follow-up of the MARIPOSA Study

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Key Takeaway

Amivantamab + lazertinib is US Food and Drug Administration (FDA) approved for first-line epidermal growth factor (EGFR)-mutant non-small cell lung cancer (NSCLC) and is improving long-term outcomes vs osimertinib, based on its multitargeted mechanism and blocking of EGFR and mesenchymal epithelial transition (MET) receptors with immune cell-directing activity

Conclusions

After longer follow-up (median: 31.1 months), data continue to favor first-line amivantamab + lazertinib over osimertinib with a promising overall survival (OS) trend (hazard ratio [HR], 0.77; $P=0.019$) in patients with EGFR-mutant advanced NSCLC – OS curves separate early and widen over time, favoring amivantamab + lazertinib – 61% of patients receiving amivantamab + lazertinib were alive at 3 years vs 53% for osimertinib – This analysis was requested by health authorities and had nominal alpha spend. A P -value of ≤ 0.00001 was required for statistical significance

First-line amivantamab + lazertinib showed reduced risk of central nervous system (CNS) progression and sustained CNS control with more durable responses – 3-year intracranial progression-free survival (icPFS) was double for amivantamab + lazertinib vs osimertinib (38% vs 18%) – Amivantamab + lazertinib showed a favorable trend for intracranial duration of response (icDoR; not estimable [NE] vs 24.4 months)

Post-progression outcomes (time to treatment discontinuation [TTD], time to subsequent treatment [TTST], and progression-free survival after subsequent therapy [PFS2]) were significantly improved with first-line amivantamab + lazertinib vs osimertinib

The MARIPOSA study is ongoing, and a prespecified final OS analysis with formal statistical testing will be conducted in the future

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Background

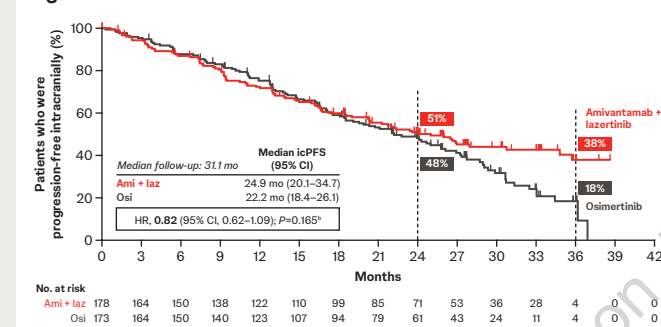
- First-line treatment of EGFR-mutant advanced NSCLC with 3rd-generation EGFR tyrosine kinase inhibitors (TKIs) has shown a median OS of ~3 years,^{1,2} with an estimated real-world 5-year survival of <20%³
- Approximately 25%–40% of patients do not receive second-line therapy,^{4–6} indicating a need for improved first-line treatments
- Amivantamab is an EGFR-MET bispecific antibody with immune cell-directing activity,^{7–9} and lazertinib is a 3rd-generation EGFR TKI^{10,11}
- At a median follow-up of 22.0 months, amivantamab + lazertinib significantly improved PFS vs osimertinib in the first-line setting (HR, 0.70; 95% confidence interval [CI], 0.58–0.85; $P<0.001$) in MARIPOSA^{12,13}
 - At the first interim OS analysis, a trend in OS was seen favoring amivantamab + lazertinib vs osimertinib (HR, 0.80; 95% CI, 0.61–1.05; $P=0.11$)^{12,13}
- Amivantamab + lazertinib was recently approved by the FDA for first-line treatment of patients with common EGFR-mutant advanced NSCLC¹⁴
- Here, we report longer-term follow-up (median: 31.1 months) of amivantamab + lazertinib vs osimertinib from MARIPOSA

Results

icPFS

- MARIPOSA required serial brain imaging for all patients, which provides robust evaluation of CNS outcomes
- Amivantamab + lazertinib showed a favorable trend in icPFS with sustained and durable CNS control at 3 years (Figure 2)
 - 3-year landmark icPFS was double for amivantamab + lazertinib vs osimertinib (38% vs 18%)

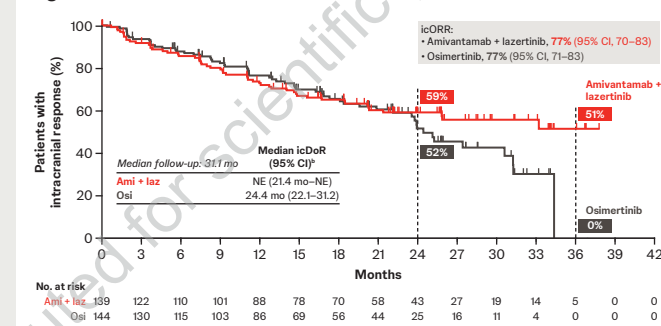
Figure 2: icPFS^a



icDoR

- Intracranial objective response rate (icORR) was 77% for both arms
- However, amivantamab + lazertinib demonstrated greater durability of response, with improved icDoR vs osimertinib (Figure 3)

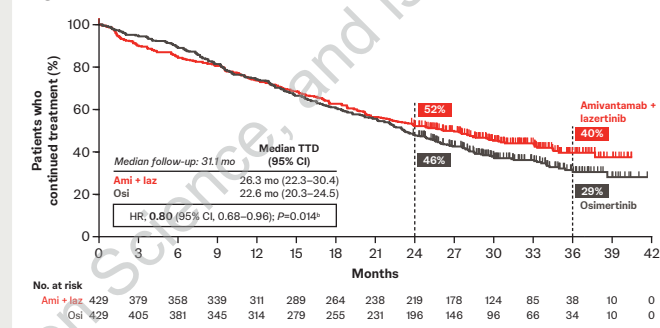
Figure 3: icDoR^a



TTD

- Amivantamab + lazertinib demonstrated significantly longer TTD vs osimertinib (Figure 4)
 - More patients remained on treatment at 3 years with amivantamab + lazertinib (40% vs 29%)

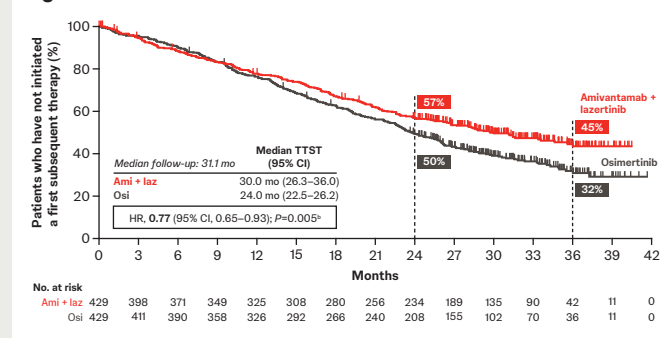
Figure 4: TTD^a



TTST

- Amivantamab + lazertinib had significantly longer TTST (Figure 5)
 - Fewer patients at the 3-year landmark on the amivantamab + lazertinib arm started a subsequent therapy versus osimertinib (45% vs 32%)

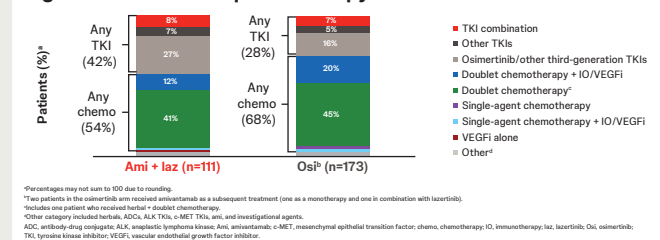
Figure 5: TTST^a



First Subsequent Therapy

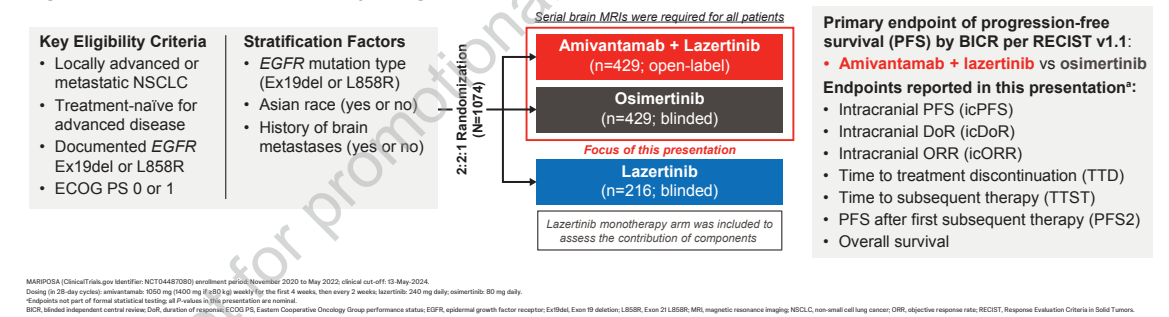
- Among patients with progressive disease who discontinued treatment, the proportion of patients that went on to receive subsequent therapy was similar between arms (amivantamab + lazertinib: 72% vs osimertinib: 74%; Figure 6)
 - The majority of patients who discontinued study treatment received second-line therapy, with chemotherapy being the most common subsequent therapy class in both arms

Figure 6: First Subsequent Therapy



Methods

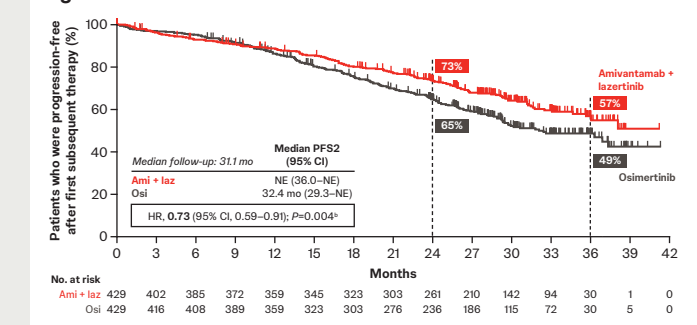
Figure 1: Phase 3 MARIPOSA study design



PFS2

- Amivantamab + lazertinib significantly reduced the risk of 2nd disease progression or death by 27% (Figure 7)
 - 3-year landmark PFS2 was 57% for amivantamab + lazertinib vs 49% for osimertinib

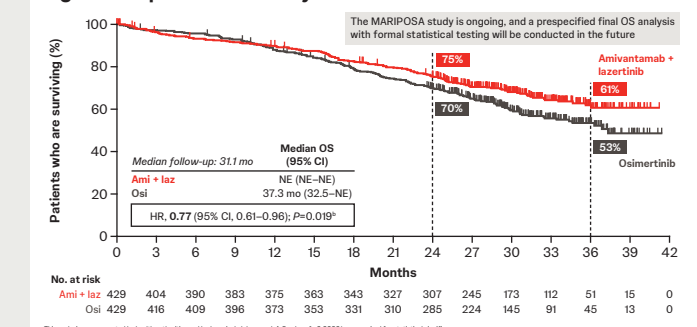
Figure 7: PFS2^a



Updated OS Analysis

- A strong OS trend favoring amivantamab + lazertinib was observed (Figure 8)
 - OS curves separate early and widen over time favoring amivantamab + lazertinib, with 61% of patients alive at 3 years vs 53% with osimertinib

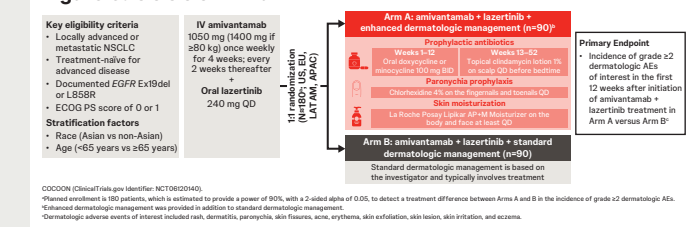
Figure 8: Updated OS Analysis^a



COCOON Trial

- The COCOON Trial aims to reduce dermatologic adverse events associated with first-line amivantamab + lazertinib (Figure 9)

Figure 9: COCOON Trial



Lung Cancer