MARIPOSA Phase 3 Study: Efficacy & Safety

Intravenous Amivantamab Plus Lazertinib in Previously Untreated Locally Advanced or Metastatic NSCLC with *EGFR* Exon 19 Deletions or Exon 21 L858R Substitution Mutations

MARIPOSA Study Design[1,2]

Key Eligibility Criteria[1]
- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R, ECOG PS 0 or 1
- Asymptomatic or previously treated and stable intracranial metastases were eligible to enroll.

Stratification Factors[1]
- *EGFR* mutation type (Ex19del or L858R)
- Asian race (yes or no)
- History of brain metastases (yes or no)

2:2:1 Randomization (N=1074)

Serial brain MRIs were required for all patients[1]

- **Amivantamab + lazertinib** (n=429; open-label)
- **Osimertinib** (n=429; blinded)
- **Lazertinib** (n=216; blinded)

Dosing
Amivantamab: 1050/1400 mg* IV, QW for weeks 1 to 5, and then Q2W starting at Week 7
Lazertinib: 240 mg PO QD

Primary endpoint of PFS by BICR per RECIST v1.1:[2]
- Amivantamab + lazertinib vs osimertinib

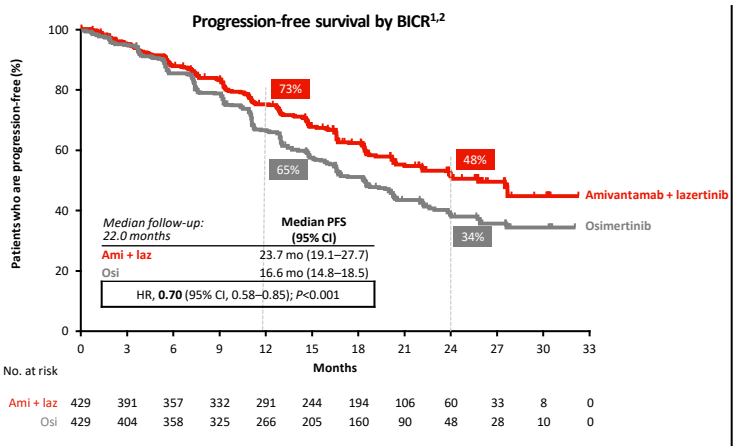
Key Secondary endpoints:[2,3]
- OS‡
- ORR
- DOR
- Intracranial PFS‡

Key exploratory endpoints:[3-5]
- Intracranial DOR and ORR by BICR‡

Lazertinib monotherapy was included to assess the contribution of the component[3]

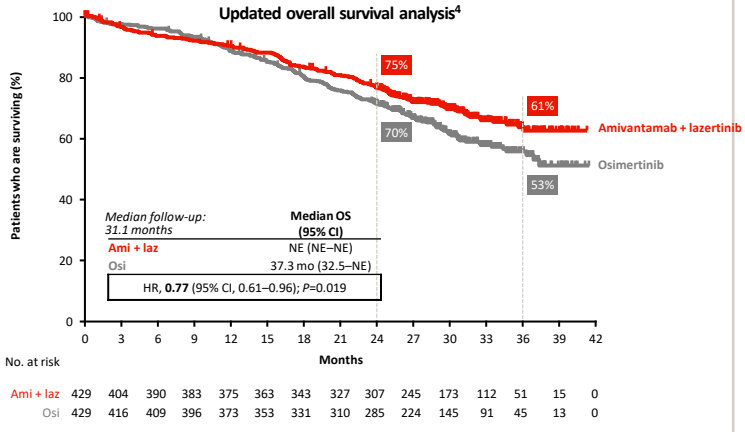
Efficacy Outcomes[1,2,4]

Progression-free survival by BICR[1,2]



- At a median follow-up of 22.0 months, amivantamab + lazertinib reduced the risk of progression or death by 30% and significantly improved PFS versus osimertinib

Updated overall survival analysis[4]



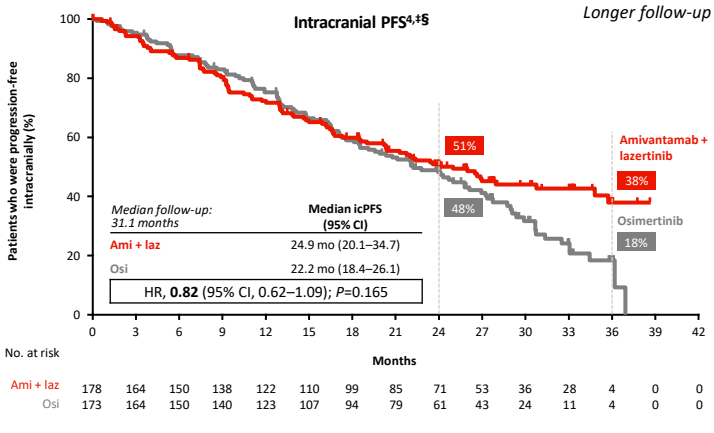
The P-value displayed is nominal, and statistical significance has not been established.

	ORR[2] %, (95% CI)		DoR[2] Median, months (95% CI)	
Amivantamab + lazertinib (n=429)	78% (95% CI: 74–82)		25.8 months (95% CI: 20.1–NE)	
	CR: 5.4%	PR: 73%	DoR ≥6 months: 86%	DoR ≥12 months: 68%
Osimertinib (n=429)	73% (95% CI: 69–78)		16.7 months (95% CI: 14.8–18.5)	
	CR: 3.5%	PR: 70%	DoR ≥6 months: 85%	DoR ≥12 months: 57%

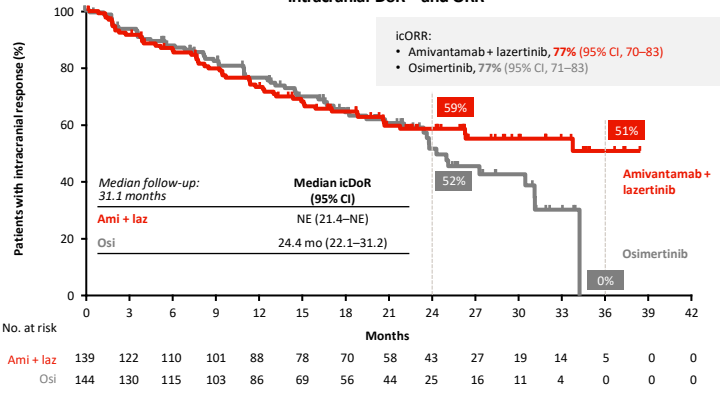
CNS Efficacy Outcomes[4,‡]

Longer follow-up (median: 31.1 months)

Intracranial PFS[4,‡§]



Intracranial DoR[‡¶] and ORR[4,‡]



These endpoints were not adjusted for multiple comparisons; P-values displayed are nominal, and statistical significance has not been established.

*1400-mg doses for patients with body weight 80 kg or greater. ‡Endpoints are reported from a non-prespecified data cut off. §Intracranial PFS was defined as time from randomization until the date of intracranial disease progression (progression of brain metastasis or occurrence of new brain lesions) or death, based on BICR using RECIST v1.1 among patients with a history of brain metastases. Baseline brain MRI was required for all patients and performed ≤28 days prior to randomization; patients who could not have MRIs were allowed to have CT scans. Brain scan frequency was every 8 weeks for the first 30 months, then every 12 weeks thereafter for patients with a history of brain metastasis and every 24 weeks for patients with no history of brain metastasis. ¶Intracranial DoR was defined as the time from the date of first documented intracranial response (CR or PR) until the date of documented intracranial progression or death, whichever occurred first, among patients with a history of brain metastases at screening who have intracranial CR or PR based on BICR using RECIST v1.1.

Ami + laz, amivantamab + lazertinib; BICR, blinded independent central review; C, cycle; CI, confidence interval; CNS, central nervous system; CR, complete response; D, day; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, Exon 19 deletion; ic, intracranial; IV, intravenous; L858R, Exon 21 L858R; NE, not estimable; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; osi, osimertinib; PFS, progression-free survival; PFS2, PFS after first subsequent therapy; PO, oral; PR, partial response; Q2W, every 2 weeks; QD daily; QW, weekly; RECIST, Response Evaluation Criteria in Solid Tumors; TTD, time to treatment discontinuation; TTSP, time to symptomatic progression; TTST, time to subsequent therapy.

1. Cho BC, et al. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614. 2. RYBREVANT® (amivantamab-vmjw) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 3. Cho BC, et al. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614. (Supplementary Protocol) 4. Gadgeel S, et al. Presented at World Conference on Lung Cancer (WCLC) Congress 2024, September 7–10, 2024; San Diego, CA, USA. OA02.03. 5. Felip E, et al. *Ann Oncol*. 2024. doi:10.1016/j.annonc.2024.05.541.

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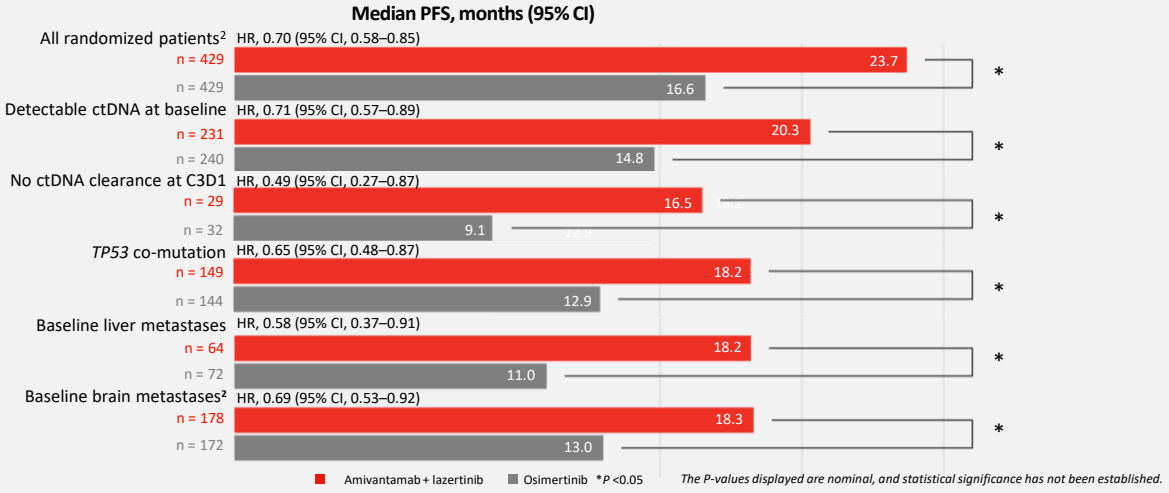
Efficacy in Patients with High-risk Features[1]

(secondary analysis from MARIPOSA)

In the MARIPOSA study, 89% of patients had ≥1 high-risk feature detected at baseline

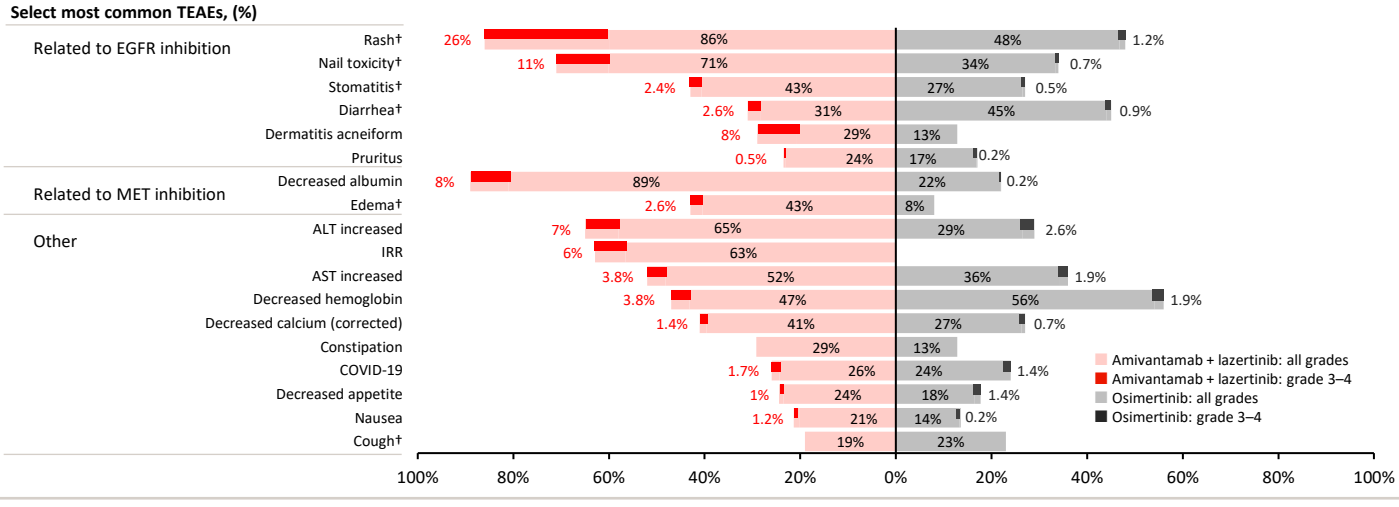
- ctDNA was detected by NGS in 85% of patients which remained persistent at C3D1 in 15% of patients
- *TP53* co-mutations were detected in 54% of patients while baseline liver and brain metastases were detected in 16% and 41% of patients, respectively



Safety[2-4]

- Safety profile of amivantamab + lazertinib was consistent with prior reports, mostly grades 1–2[2,3]

These data reflect exposure to amivantamab in combination with lazertinib in 421 patients[2,3]



Adverse reactions: Amivantamab[3]

Adverse reactions: Lazertinib[4]

These data reflect exposure to amivantamab in combination with lazertinib in 421 patients[3,4]

Serious adverse reactions

49%

In ≥2% of patients:

VTE (11%), pneumonia (4%), rash and ILD/pneumonitis (2.9% each), COVID-19 (2.4%), pleural effusion, and IRR (2.1% each)

Permanent discontinuation

34%

In ≥1% of patients:

Rash, IRR, nail toxicity, VTE, ILD/pneumonitis, pneumonia, edema, hypoalbuminemia, fatigue, paresthesia, and dyspnea

Dose interruptions

88%

In ≥5% of patients:

IRR, rash, nail toxicity, COVID-19, VTE, increased ALT, edema, and hypoalbuminemia

Dose reductions

46%

In ≥5% of patients:

Rash and nail toxicity

Permanent discontinuation

21%

In ≥1% of patients:

ILD/pneumonitis, pneumonia, VTE, rash, respiratory failure, and sudden death

Dose interruptions

72%

In ≥5% of patients:

Rash, nail toxicity, COVID-19, VTE, increased ALT, and increased AST

Dose reductions

42%

In ≥5% of patients:

Rash and nail toxicity

Fatal adverse reactions occurred in **7% of patients** who received amivantamab in combination with lazertinib due to death not otherwise specified (1.2%); sepsis and respiratory failure (1% each); pneumonia, myocardial infarction and sudden death (0.7% each); cerebral infarction, pulmonary embolism, and COVID-19 infection (0.5% each); and ILD/pneumonitis, acute respiratory distress syndrome, and cardiopulmonary arrest (0.2% each).

Johnson & Johnson

†Grouped terms.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; C, cycle; CI, confidence interval; ctDNA, circulating tumor DNA; D, day; EGFR, epidermal growth factor receptor; HR, hazard ratio; ILD, interstitial lung disease (includes pneumonitis); IRR, infusion-related reaction; NGS, next generation sequencing; OS, overall survival; TEAE, treatment-emergent adverse event; VTE, venous thromboembolism.

1. Felip E, et al. *Ann Oncol*. 2024. doi: 10.1016/j.annonc.2024.05.541. 2. Cho BC, et al. *N Engl J Med.* 2024. doi:10.1056/NEJMoa2403614. 3. RYBREVANT® (amivantamab-vmjw) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 4. LAZCLUZE™ (lazertinib) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc.