MARIPOSA
1L *EGFR*+ NSCLC

Lazertinib vs Osimertinib in 1L *EGFR*-mutant Advanced NSCLC: A Randomized, Double-blind, Exploratory Analysis From MARIPOSA

Se-Hoon Lee[1], Byoung Chul Cho[2], Hidetoshi Hayashi[3], Enriqueta Felip[4], Alexander I Spira[5], Nicolas Girard[6], Yu Jung Kim[7], Yuriy Ostapenko[8], Pongwut Danchaivijitr[9], Baogang Liu[10], Adlinda Alip[11], Ernesto Korbenfeld[12], Josiane Mourão Dias[13], Ki Hyeong Lee[14], Hailin Xiong[15], Soon Hin How[16], Ying Cheng[17], Gee-Chen Chang[18], James Chih-Hsin Yang[19], Benjamin Besse[20], Michael Thomas[21], Joshua C Curtin[22], Jiarui Zhang[22], John Xie[23], Tao Sun[23], Melissa Martinez[23], Seema Sethi[22], Roland E Knoblauch[22], Elizabeth Fennema[24], Mahesh Daksh[23], Mariah Ennis[22], Joshua M Bauml[22], Shun Lu[25]

[1]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [2]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [3]Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka, Japan; [4]Medical Oncology Service, Vall d'Hebron Institute of Oncology (VIHO), Vall d'Hebron Barcelona Hospital Campus, Universitat Autonoma de Barcelona, Barcelona, Spain; [5]Virginia Cancer Specialists, Fairfax, VA, USA; [6]Institut du Thorax Curie-Montsouris, Paris, France; Paris Saclay University, UVSQ, Versailles, France; [7]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea; [8]National Cancer Institute, Kyiv, Ukraine; [9]Siriraj Hospital, Mahidol University Bangkok Noi Campus, Bangkok, Thailand; [10]Harbin Medical University Cancer Hospital, Harbin, China; [11]Clinical Oncology Unit, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; [12]British Hospital of Buenos Aires – Central British Hospital, Buenos Aires, Argentina; [13]Department of Medical Oncology, Barretos Cancer Hospital, São Paulo, Brazil; [14]Medical Department, Chungbuk National University Hospital, Cheongju, Republic of Korea; [15]Huizhou Municipal Central Hospital of Guangdong Province, Huizhou, China; [16]International Islamic University Malaysia (IIUM) Medical Specialist Centre, Pahang, Malaysia; [17]Jilin Cancer Hospital, Changchun, China; [18]Chung Shan Medical University, Chung Shan Medical University Hospital, Taichung, Taiwan; [19]National Taiwan University Cancer Center, Taipei, Taiwan; [20]Paris-Saclay University, Institut Gustave Roussy, Villejuif, France; [21]Department of Thoracic Oncology, Thoraxklinik, Heidelberg University Hospital and National Center for Tumor Diseases, NCT Heidelberg, a partnership between DKFZ and Heidelberg University Hospital, Heidelberg, Germany; Translational Lung Research Center Heidelberg (TLRC-H), Member of the German Center for Lung Research (DZL); [22]Janssen Research & Development, Spring House, PA, USA; [23]Janssen Research & Development, Raritan, NJ, USA; [24]Janssen Research & Development, San Diego, CA, USA; [25]Shanghai Lung Cancer Center, Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

MARIPOSA
1L *EGFR*+ NSCLC

Background

- Lazertinib is a highly selective, CNS-penetrant, third-generation EGFR-TKI[1]
- Lazertinib was superior to gefitinib in treatment-naïve *EGFR*-mutant advanced NSCLC in the LASER301 study (HR, 0.45; 95% CI, 0.34–0.58; *P*<0.001)[1]
- Lazertinib was selected for combination with amivantamab due to:
  - High selectivity for mutant EGFR, with relatively low rates of wild-type EGFR toxicity[1–3]
  - Minimal inhibition of HER2, without elevated risk of QTc prolongation or cardiomyopathy[1–3]
- In MARIPOSA, amivantamab + lazertinib demonstrated superior PFS versus osimertinib (HR, 0.70; 95% CI, 0.58–0.85; *P*<0.001), leading to its FDA approval for patients with treatment-naïve *EGFR*-mutant advanced NSCLC[4–6]

We compared single-agent lazertinib versus osimertinib: A randomized, double-blind, exploratory analysis

CI, confidence interval; CNS, central nervous system; EGFR, epidermal growth factor receptor; HR, hazard ratio; NSCLC, non-small cell lung cancer; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

1. Cho BC, et al. *J Clin Oncol*. 2023;41(26):4208–4217. 2. Heppner DE, et al. *ACS Med Chem Lett*. 2022;13(12):1856–1863. 3. Yun J, et al. *Clin Cancer Res*. 2019;25(8):2575–2587. 4. Cho BC, et al. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2403614. 5. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024. 6. LAZCLUZE® (lazertinib) tablets, for oral use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024.

MARIPOSA: Phase 3 Study Design

MARIPOSA
1L *EGFR*+ NSCLC

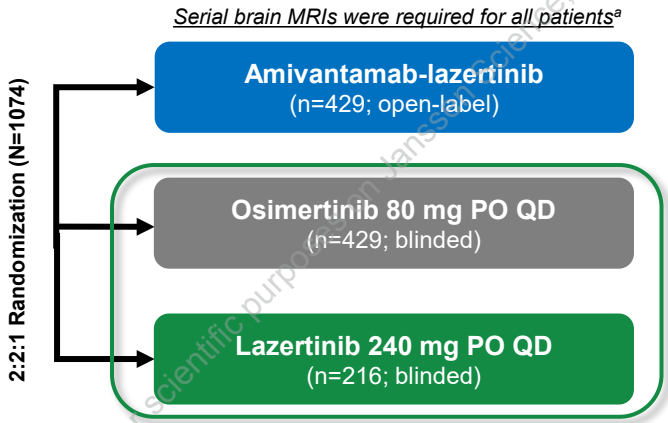
This is the first randomized, double-blind trial to prospectively evaluate 2 third-generation EGFR-TKIs

Key eligibility criteria

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0 or 1
- Asymptomatic brain metastases did not require definitive treatment

Stratification factors

- *EGFR* mutation type (Ex19del or L858R)
- Asian race (yes or no)
- History of brain metastases (yes or no)



Primary endpoint: PFS by BICR per RECIST v1.1:

- **Amivantamab-lazertinib** vs **osimertinib**

Exploratory endpoints for lazertinib vs osimertinib reported here:

- PFS by BICR per RECIST v1.1
- ORR
- DoR
- TTSP
- OS
- Safety

Lazertinib monotherapy arm was included to assess the contribution of components

Note: MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080) enrollment period: November 2020 to May 2022; clinical cut-off: 11-Aug-2023.

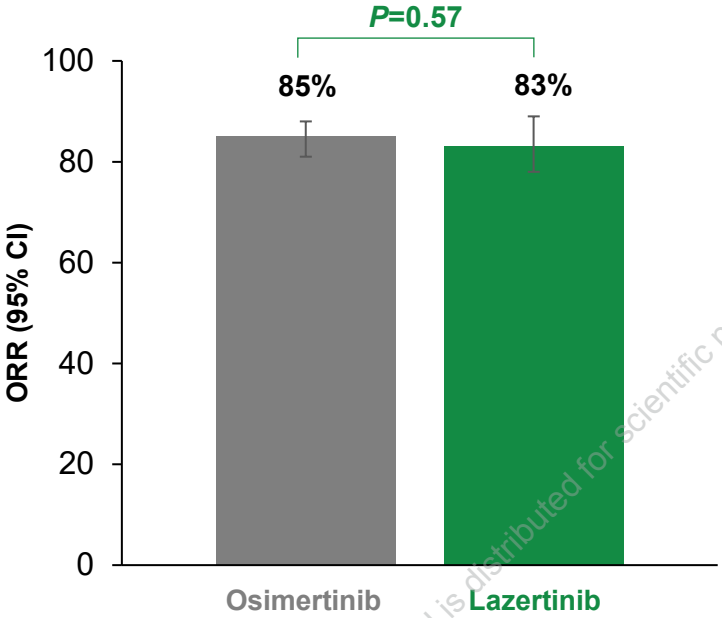
[a]Baseline brain MRIs were required for all patients and performed ≤28 days prior to randomization; patients who could not have MRIs were permitted to have CT scans. Brain scan frequency was every 8 weeks for the first 30 months and then every 12 weeks thereafter for patients with a history of brain metastasis and every 24 weeks for patients with no history of brain metastasis. Extracranial tumor assessments were conducted every 8 weeks for the first 30 months and then every 12 weeks until disease progression was confirmed by BICR.

BICR, blinded independent central review; CT, computed tomography; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor; TTSP, time to symptomatic progression.

MARIPOSA
1L *EGFR*+ NSCLC

ORR and DoR by BICR

ORR and median DoR were comparable between lazertinib and osimertinib



BICR-assessed response, n (%)[a]	Osimertinib (n=429)	Lazertinib (n=216)
ORR		
All responders	85% (95% CI, 81–88)	83% (95% CI, 77–88)
Confirmed responders	76% (95% CI, 71–80)	75% (95% CI, 68–80)
Best response[b]		
CR	15 (4)	9 (4)
PR	335 (81)	168 (79)
SD	42 (10)	23 (11)
PD	11 (3)	9 (4)
NE	11 (3)	5 (2)
Median DoR[c]	16.8 mo (95% CI, 14.8–18.5)	16.6 mo (95% CI, 14.8–20.2)
Ongoing responses	151 of 314 (48)	77 of 160 (48)

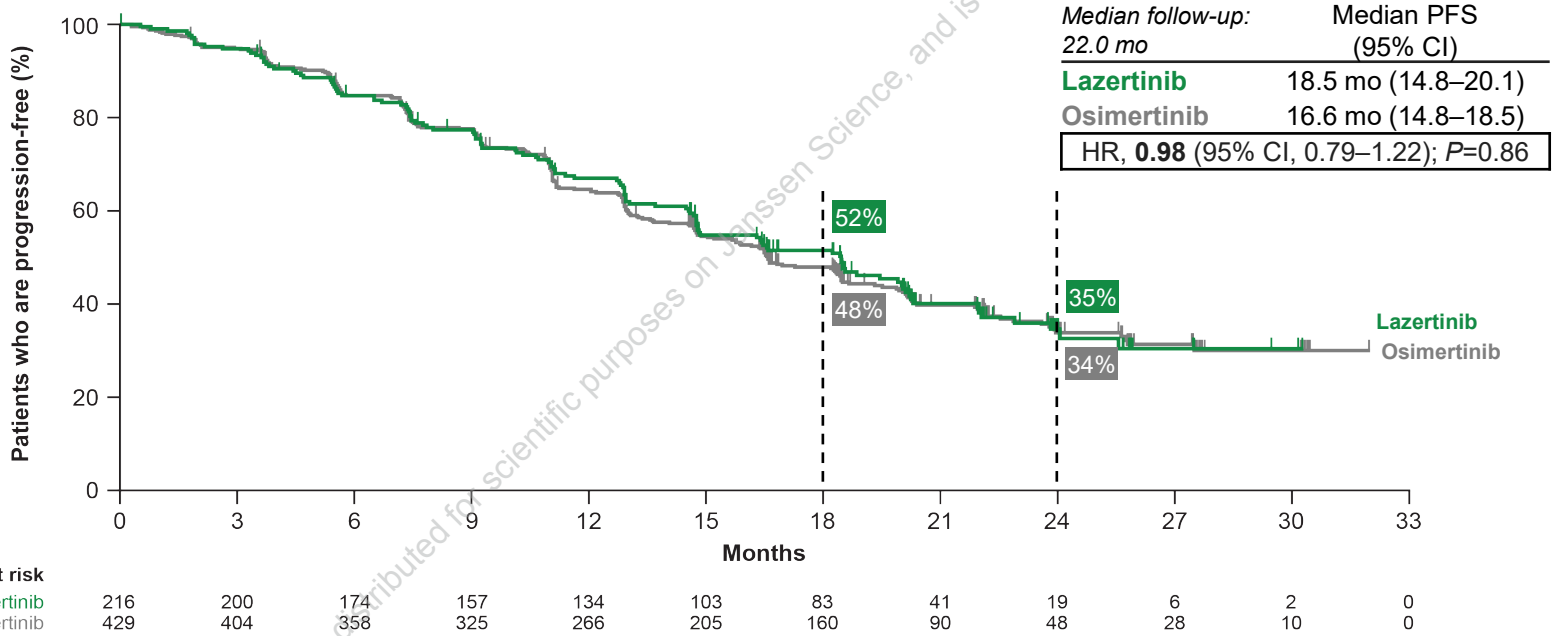
[a]No. of patients with measurable disease at baseline by BICR was 214 for lazertinib and 414 for osimertinib. [b]Includes all responders. [c]Among confirmed responders.

BICR, blinded independent central review; CI, confidence interval; CR, complete response; DoR, duration of response; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

MARIPOSA
1L *EGFR*+ NSCLC

PFS by BICR

PFS was comparable between the lazertinib and osimertinib arms



- PFS was comparable between lazertinib and osimertinib among prespecified subgroups including Asian race[a] and *EGFR* mutation subtype[b]

[a]HR, 1.02 (95% CI, 0.77–1.35). [b]Exon 19 deletion: HR, 1.03 (95% CI, 0.78–1.37); L858R: HR, 0.91 (95% CI, 0.65–1.28).

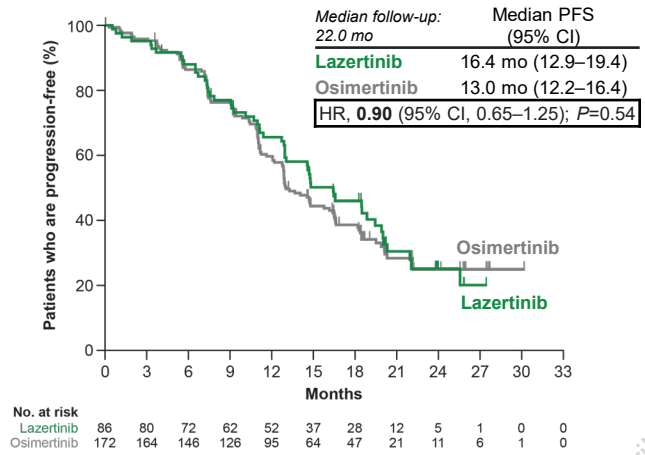
BICR, blinded independent central review; CI, confidence interval; EGFR, epidermal growth factor receptor; HR, hazard ratio; PFS, progression-free survival.

MARIPOSA
1L *EGFR*+ NSCLC

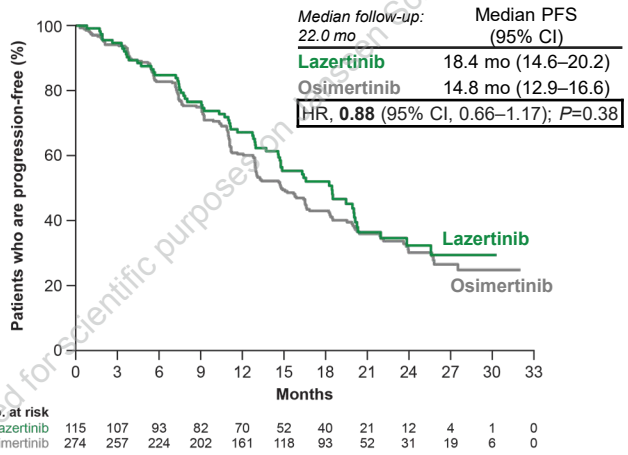
PFS by High-risk Subgroups

High-risk features, such as brain metastases, ctDNA shedding, and baseline TP53 co-mutations are common in patients with EGFR-mutated NSCLC.[1–4] PFS results in these groups were comparable across arms

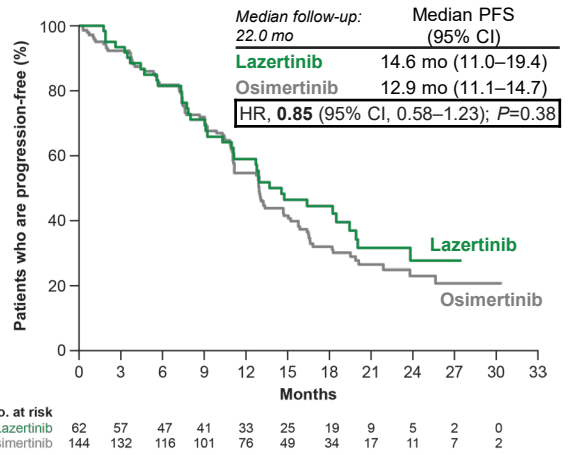
With brain metastases[a]



With detectable ctDNA at baseline[a,b]



With TP53 co-mutations[a,b]



[a]PFS was comparable for patients without a history of brain metastases (lazertinib: n=130, osimertinib: n=257; HR, 1.01 [95% CI, 0.75–1.35]), without detectable ctDNA at baseline (lazertinib: n=31, osimertinib: n=42; HR, 1.32 [95% CI, 0.99–1.75]), and for patients with wild-type *TP53* (lazertinib: n=84, osimertinib: n=172; HR, 0.95 [95% CI, 0.71–1.26]). [b]Pathogenic alterations were detected with the Guardant Health G360® panel.

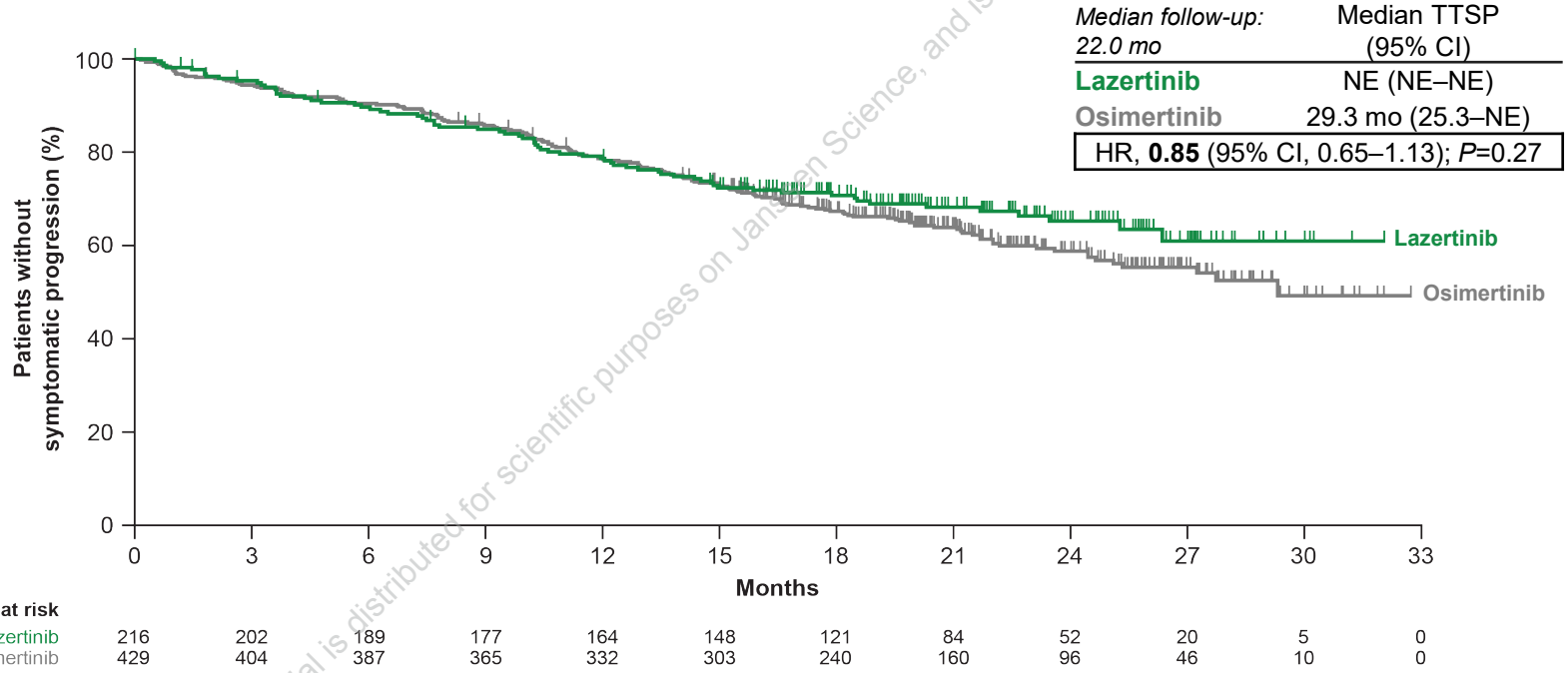
CI, confidence interval; ctDNA, circulating tumor DNA; EGFR, epidermal growth factor receptor; HR, hazard ratio; PFS, progression-free survival; NSCLC, non-small cell lung cancer.

1. Gray JE, et al. *Clin Cancer Res*. 2023;29(17):3340–3351. 2. Ma S, et al. *Transl Lung Cancer Res*. 2021;10(1):326–339. 3. Takeyasu Y, et al. *JTO Clin Res Rep*. 2024;5(2):100636. 4. Soria JC, et al. *N Engl J Med*. 2018;378(2):113–125.

MARIPOSA
1L *EGFR*+ NSCLC

Time to Symptomatic Progression[a]

Pre-planned analysis of TTSP demonstrated comparable results for lazertinib and osimertinib



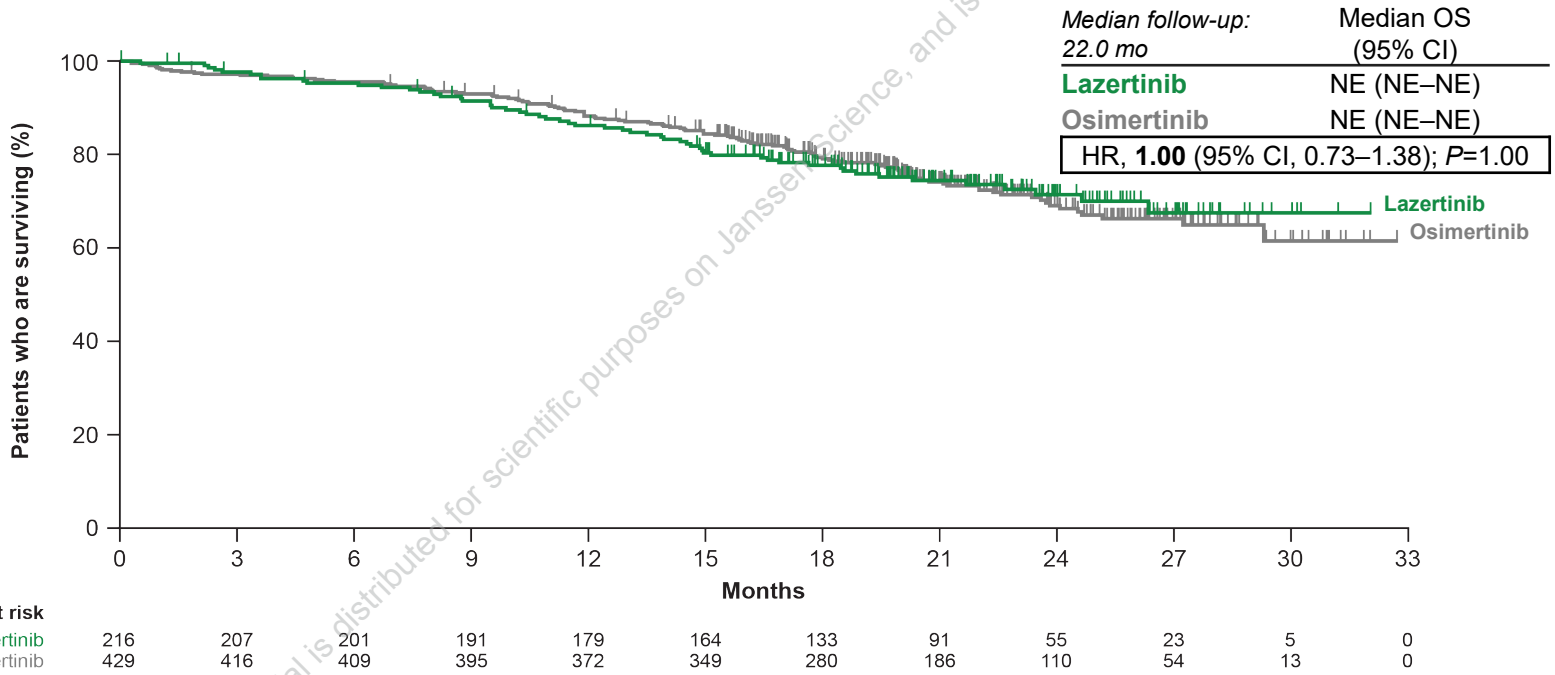
[a]Time from randomization to first onset of new/worsening of lung cancer symptoms requiring a change in therapy, clinical intervention, or death.

CI, confidence interval; HR, hazard ratio; NE, not estimable; TTSP, time to symptomatic progression.

MARIPOSA
1L *EGFR*+ NSCLC

Interim OS

Early data demonstrated comparable survival outcomes between lazertinib and osimertinib



CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival.

Safety Profile

MARIPOSA
1L *EGFR*+ NSCLC

The safety profiles for each agent were consistent with prior reports[1,2]

- Most individual TEAEs were grade 1–2 for **osimertinib** and **lazertinib**
  - Serious AEs were similar: **33%** versus **35%**
  - AEs leading to death were comparable and low: **7%** versus **6%**
  - Rates of ILD[a] were comparable and low: **3%** versus **3%**
- Osimertinib had higher rates of diarrhea (**44%** vs **32%**), thrombocytopenia (**20%** vs **9%**), and neutropenia (**13%** vs **3%**) versus lazertinib
- Lazertinib had higher rates of rash (**45%** vs **31%**), muscle spasms (**23%** vs **7%**), and paresthesia (**15%** vs **6%**) versus osimertinib
- Treatment-related discontinuations were comparable and low: **3%** versus **5%**

Most common TEAEs (≥20%) by preferred term, n (%)	Osimertinib (n=428)		Lazertinib (n=213)	
Related to EGFR inhibition	Grade 1–2	Grade ≥3	Grade 1–2	Grade ≥3
Diarrhea	187 (44)	3 (1)	64 (30)	4 (2)
Rash	128 (30)	3 (1)	91 (43)	4 (2)
Paronychia	119 (28)	2 (0.5)	59 (28)	2 (1)
Stomatitis	89 (21)	1 (0.2)	37 (17)	1 (0.5)
Dermatitis acneiform	55 (13)	0	45 (21)	0
Other				
COVID-19	94 (22)	9 (2)	39 (18)	3 (1)
Cough	88 (21)	0	36 (17)	1 (0.5)
Anemia	84 (20)	7 (2)	40 (19)	3 (1)
Thrombocytopenia	79 (18)	5 (1)	19 (9)	1 (0.5)
AST increased	53 (12)	5 (1)	42 (20)	3 (1)
ALT increased	49 (11)	8 (2)	44 (21)	6 (3)
Muscle spasms	32 (7)	0	49 (23)	1 (0.5)

[a]Includes ILD and pneumonitis.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EGFR, epidermal growth factor receptor; ILD, interstitial lung disease; TEAE, treatment-emergent adverse event.

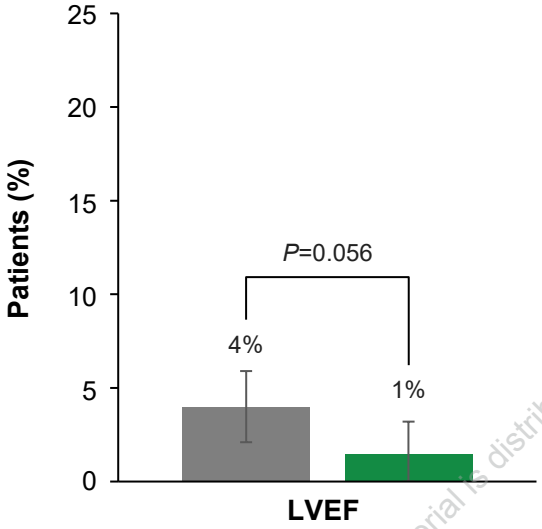
1. Cho BC, et al. *J Clin Oncol*. 2023;41(26):4208–4217. 2. Soria JC, et al. *N Engl J Med*. 2018;378(2):113–125.

MARIPOSA
1L *EGFR*+ NSCLC

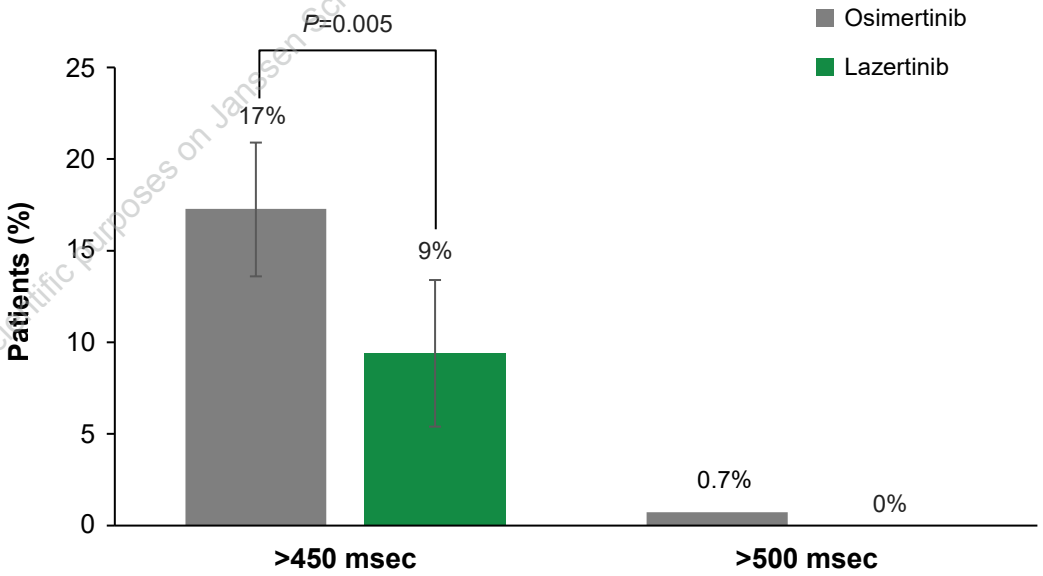
LVEF Worsening and QT Interval Prolongation

Lazertinib had a reduced risk of cardiomyopathy and significantly lowered rates of QT interval prolongation versus osimertinib

Percentage of patients with LVEF <LLN and >10% absolute decrease from baseline



Percentage of patients with QT interval >450 and >500 msec[a]



[a]Maximum postbaseline values.

LLN, lower limit of normal; LVEF, left ventricular ejection fraction.

MARIPOSA
1L *EGFR*+ NSCLC

Conclusions

- Lazertinib demonstrated comparable efficacy versus osimertinib across all clinical endpoints, including in high-risk subgroups
- Safety profiles of both lazertinib and osimertinib included mostly grade 1–2 AEs with low and comparable rates of treatment-related discontinuations
- Consistent with lazertinib's suitable combinability profile, key safety distinctions between lazertinib and osimertinib include:
  - Lower rates of diarrhea, thrombocytopenia, and neutropenia with lazertinib
  - Higher rates of rash, muscle spasms, and paresthesia with lazertinib
  - Lower rates of QT interval prolongation and cardiomyopathy with lazertinib

Lazertinib in combination with amivantamab is now FDA approved for patients with treatment-naïve, *EGFR*-mutant advanced NSCLC[1,2]

AE, adverse event; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor.

1. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024. 2. LAZCLUZE® (lazertinib) tablets, for oral use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024.

Other Amivantamab Presentations at WCLC 2024

MARIPOSA
1L *EGFR*+ NSCLC

MARIPOSA

Longer follow-up of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 10:47-10:57am
(OA02.03; Gadgeel)

PAPILLON

High-risk biomarker subpopulations from patients with *EGFR* Ex20ins in PAPILLON

Tuesday, Sep 10 1:50-1:55pm
(MA12.06; Goldman)

MARIPOSA

Patient-relevant outcomes of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Tuesday, Sep 10 1:55-2:00pm
(MA12.07; Nguyen)

SKIPPirr

Preventing infusion-related reactions with intravenous amivantamab: primary results

Tuesday, Sep 10 2:00-2:05pm
(MA12.08; Lopes)

PALOMA-3

Subcutaneous vs intravenous amivantamab: patient satisfaction and resource utilization results

Monday, Sep 9 11:07-11:17am
(OA09.05; Alexander)

EGFR esisters

Development of a **patient-friendly lung cancer lexicon**:

Sunday, Sep 8 6:15-7:45pm
(P2.16F.03; Feldman)

Poster tour: Monday, Sep 9 6:45-6:53pm

Additional posters:

- **COCOON TiP:** Enhanced vs standard dermatologic management with amivantamab + lazertinib in advanced NSCLC**:** Monday, Sep 9 12:00-2:00pm (P3.12D.04; Cho)
- **PolyDamas TiP:** Amivantamab + cetrelimab in advanced NSCLC: Virtual ePoster (EP.12H.02; Voon)
- 5-year survival estimates with 1L osimertinib for *EGFR*-mutant advanced NSCLC in the US: Virtual ePoster (EP.12A.03; Sabari)

MARIPOSA
1L *EGFR*+ NSCLC

Acknowledgments

- Patients who participated in the study and their families and caregivers
- Physicians and nurses who cared for patients, and the staff members who supported this clinical trial
- Staff members at the study sites and involved in data collection/analyses
- Medical writing assistance was provided by Lumanity Communications Inc., and was funded by Janssen Global Services, LLC

A total of 1074 patients from 27 countries were randomized in the MARIPOSA study