MARIPOSA
Ami + Laz in 1L *EGFR*+ NSCLC

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

Shirish M Gadgeel[1], Byoung Chul Cho[2], Shun Lu[3], Enriqueta Felip[4], Hidetoshi Hayashi[5], Alexander I Spira[6], Benjamin Besse[7], Michael Thomas[8], Scott Owen[9], Yu Jung Kim[10], Se-Hoon Lee[11], Josiane Mourão Dias[12], Yun-Gyoo Lee[13], Yanqiu Zhao[14], Yong Fang[15], Nicolas Girard[16], Zhe Liu[17], Ping Sun[18], Sulene Cunha Sousa Oliveira[19], Hong Shen[20], Luis Paz-Ares[21], Shingo Matsumoto[22], Hiroshi Tanaka[23], Azura Rozila Ahmad[24], Timur Andabekov[25], Patrapim Sunpaweravong[26], Ozgur Ozyilkan[27], James Chih-Hsin Yang[28], Maya Gottfried[29], Osvaldo Hernandez[30], Martin Kimmich[31], Diego Cortinovis[32], Diego Lucas Kaen[33], Lizbett Vanessa García Montes[34], Sanjay Popat[35], Thomas Newsom-Davis[36], John Xie[37], Tao Sun[37], Elizabeth Fennema[38], Mahesh Daksh[37], Mariah Ennis[39], Seema Sethi[39], Joshua M Bauml[39], Danny Nguyen[40]

[1]Division of Hematology and Oncology, Department of Internal Medicine, Henry Ford Cancer Institute/Henry Ford Health, Detroit, MI, USA; [2]Division of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea; [3]Shanghai Lung Cancer Center, Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [4]Medical Oncology Service, Vall d'Hebron Institute of Oncology (VIHO), Vall d'Hebron Barcelona Hospital Campus, Universitat Autonoma de Barcelona, Barcelona, Spain; [5]Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka, Japan; [6]Virginia Cancer Specialists, Fairfax, VA, USA; [7]Paris-Saclay University, Institut Gustave Roussy, Villejuif, France; [8]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); [9]Department of Oncology, McGill University, Montréal, QC, Canada; [10]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea; [11]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [12]Department of Medical Oncology, Barretos Cancer Hospital, São Paulo, Brazil; [13]Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [14]Department of Medical Oncology, The Affiliated Cancer Hospital of Zhengzhou University and Henan Cancer Hospital, Zhengzhou, China; [15]Department of Medical Oncology, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China; [16]Institut du Thorax Curie-Montsouris, Paris, France; Paris Saclay University, UVSQ, Versailles, France; [17]Department of Medical Oncology, Beijing Chest Hospital, Capital Medical University, Beijing, China; [18]Yantai Yuhuangding Hospital, Yantai, Shandong, China; [19]Liga Norte Riograndense Contra O Cancer, Natal - RN, Brazil; [20]The Second Affiliated Hospital of Zhejiang University College of Medicine, Hangzhou, Zhejiang, China; [21]Hospital Universitario 12 de Octubre, Madrid, Spain; [22]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [23]Department of Internal Medicine, Niigata Cancer Center Hospital, Niigata, Japan; [24]Beacon International Specialist Centre Sdn Bhd, Selangor, Malaysia; [25]Oncology Medical Clinics, AV Medical Group, St. Petersburg, Russian Federation; [26]Division of Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [27]Adana Baskent University Hospital, Ankara, Turkey; [28]Department of Medical Oncology, National Taiwan University Cancer Center, Taipei, Taiwan; [29]Meir Medical Center, Kfar-Sava, Israel; [30]Oncologia Integral Satelite, Naucalpan, Mexico; [31]Robert-Bosch-Hospital, Stuttgart, Germany; [32]SC Medical Oncology, Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy; Medicine and Surgery Department, University of Milano Bicocca, Milan, Italy; [33]Centro Oncológico Riojano Integral, La Rioja, Argentina; [34]Mexico Centre for Clinical Research, Mexico City, Mexico; [35]The Royal Marsden NHS Foundation Trust, London, UK; [36]Department of Oncology and National Centre for HIV Malignancy, Chelsea and Westminster Hospital, London, UK; [37]Janssen Research & Development, Raritan, NJ, USA; [38]Janssen Research & Development, San Diego, CA, USA; [39]Janssen Research & Development, Spring House, PA, USA; [40]City of Hope National Medical Center, Duarte, CA, USA

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Background

- First-line treatment of *EGFR*-mutant advanced NSCLC with 3rd-generation EGFR 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% CI, 0.58–0.85; *P*<0.001) in MARIPOSA[12,13]
  - At 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 NSCLC[14]

Here, we report longer-term follow-up (median: 31.1 months) of amivantamab + lazertinib vs osimertinib from MARIPOSA

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8. Vijayaraghavan S, et al. *Mol Cancer Ther*. 2020;19(10):2044-2056. 9. Yun J, et al. *Cancer Discov*. 2020;10(8):1194-1209. 10. Ahn M-J, et al. *Lancet Oncol*. 2019;20(12):1681-1690. 11. Cho BC, et al. *J Thorac Oncol*. 2022;17(4):558-567. 12. Cho BC, et al. *N Engl J Med*. 2024. doi: 10.1056/NEJMoa2403614. 13. Cho BC, et al. Presented at the European Society for Medical Oncology (ESMO) Congress; October 20-24, 2023; Madrid, Spain. 14. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024.

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Phase 3 MARIPOSA Study Design

Key Eligibility Criteria

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS 0 or 1

Stratification Factors

- *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

Amivantamab + Lazertinib (n=429; open-label)

Osimertinib (n=429; blinded)

Focus of this presentation

Lazertinib (n=216; blinded)

Lazertinib monotherapy arm was included to assess the contribution of components

Primary endpoint of progression-free survival (PFS) by BICR per RECIST v1.1:

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

Endpoints reported in this presentation[a]:

- Intracranial PFS (icPFS)
- Intracranial DoR (icDoR)
- Intracranial ORR (icORR)
- Time to treatment discontinuation (TTD)
- Time to subsequent therapy (TTST)
- PFS after first subsequent therapy (PFS2)
- Overall survival

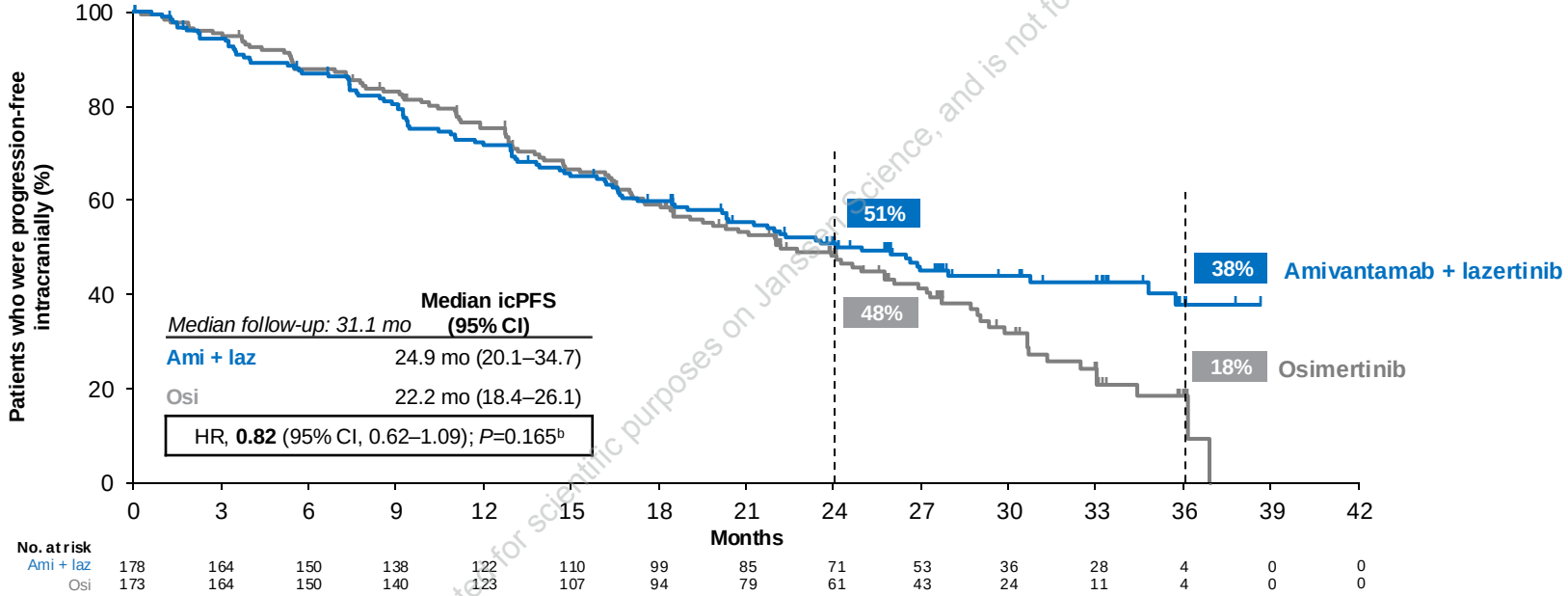
[a]Endpoints not part of formal statistical testing; all *P*-values in this presentation are nominal

MARIPOSA (ClinicalTrials.gov Identifier: NCT04487080) enrollment period: November 2020 to May 2022; clinical cut-off: 13-May-2024.
Dosing (in 28-day cycles): amivantamab: 1050 mg (1400 mg if ≥80 kg) weekly for the first 4 weeks, then every 2 weeks; lazertinib: 240 mg daily; osimertinib: 80 mg daily.

Intracranial PFS[a]

MARIPOSA required serial brain imaging for all patients, which provides robust evaluation of CNS outcomes

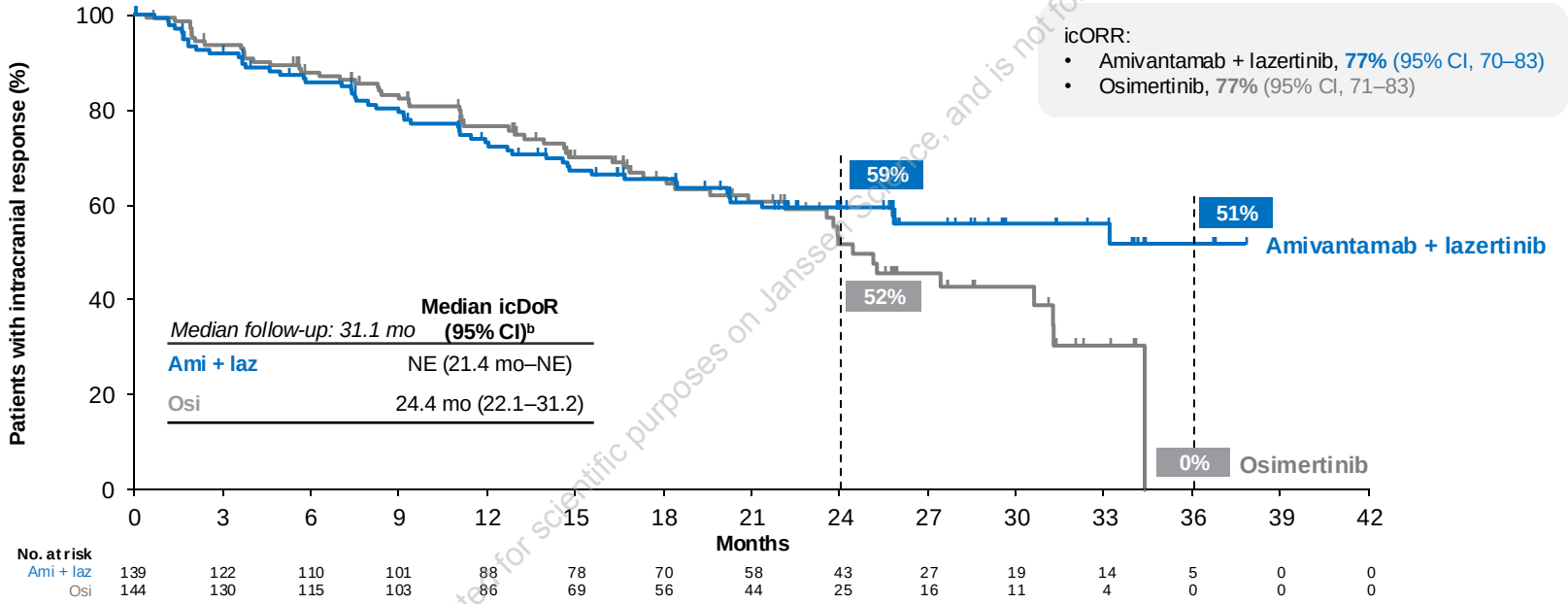
Amivantamab + lazertinib showed a favorable trend in icPFS with sustained and durable CNS control at 3 years



3-year landmark icPFS was double for amivantamab + lazertinib vs osimertinib (38% vs 18%)

[a]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. [b]*P*-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R) and race (Asian or Non-Asian). Hazard ratio was calculated from a stratified proportional hazards model.

Intracranial DoR[a]

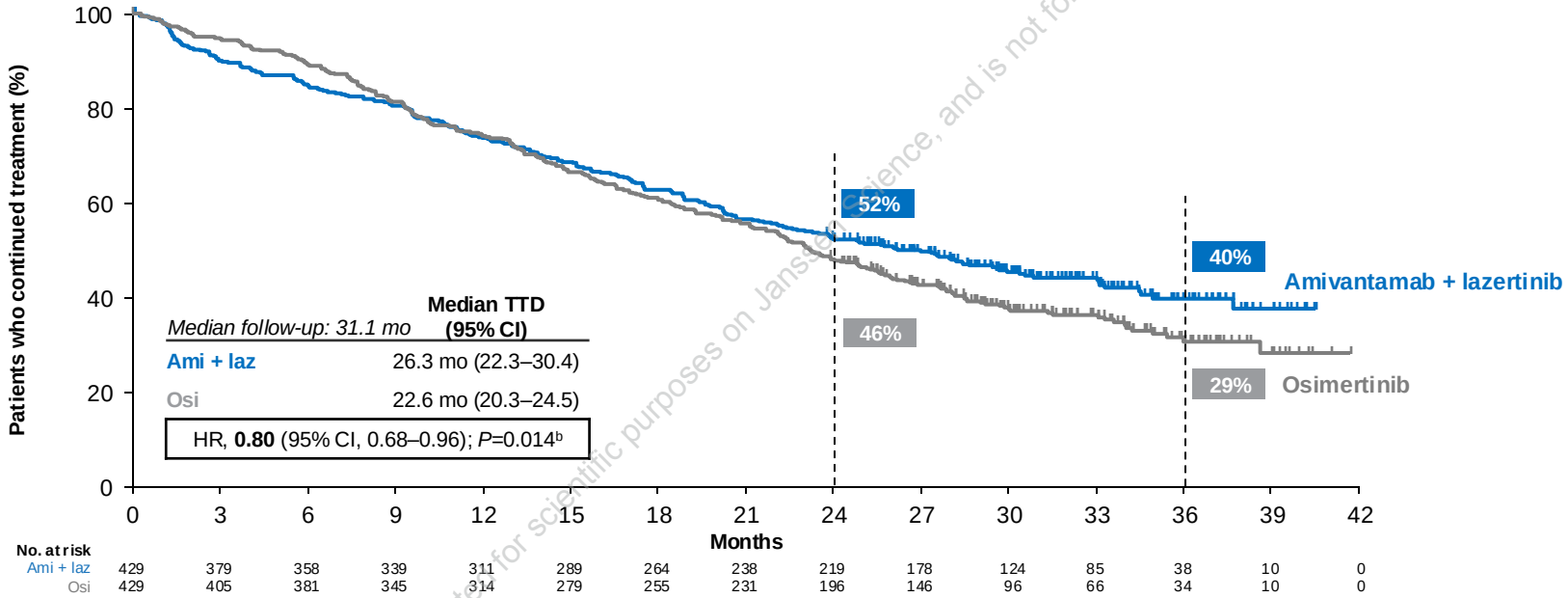


icORR was 77% for both arms; however, amivantamab + lazertinib demonstrated greater durability of response, with improved icDoR vs osimertinib

[a]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 . 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. [b]95% CIs were estimated with Kaplan-Meier method.

Time to Treatment Discontinuation[a]

Amivantamab + lazertinib demonstrated significantly longer TTD vs osimertinib

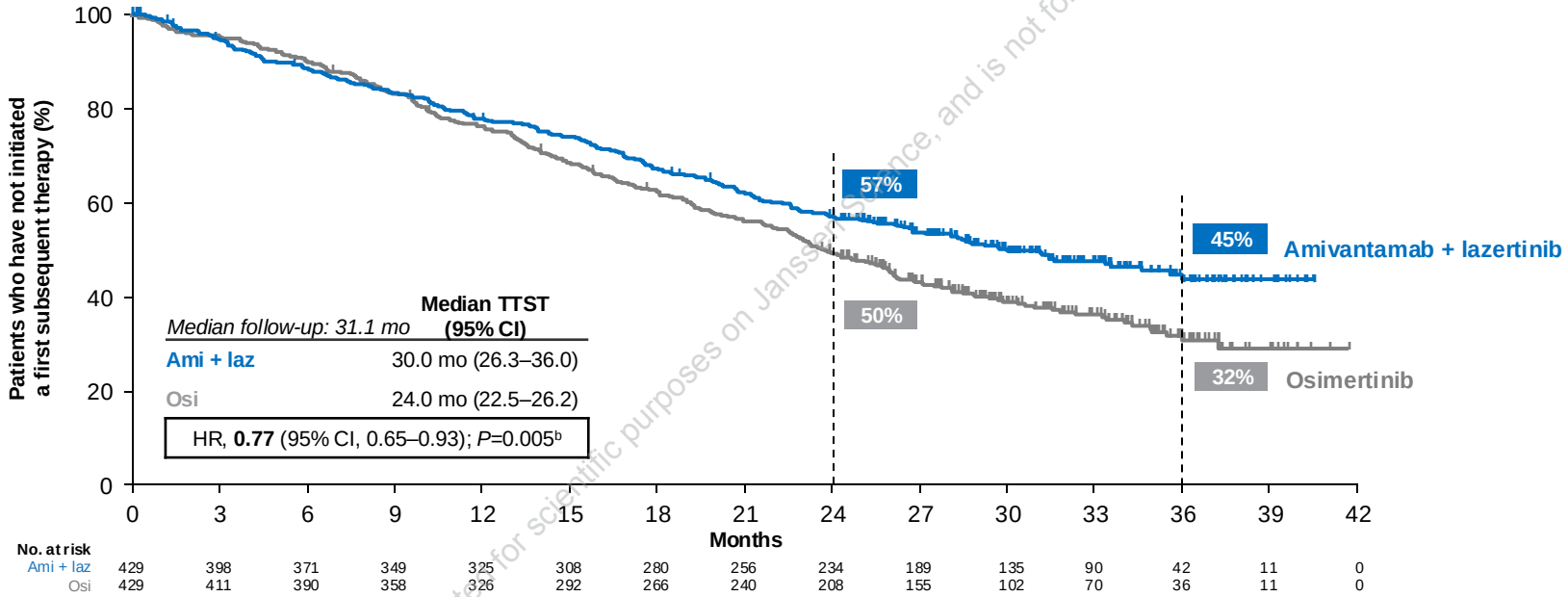


More patients remained on treatment at 3 years with amivantamab + lazertinib (40% vs 29%)

[a]TTD was defined as the time from randomization to discontinuation of treatment for any reason, including disease progression, treatment toxicity or death. [b]*P*-value is calculated by log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified proportional hazards model.

Time to Subsequent Therapy[a]

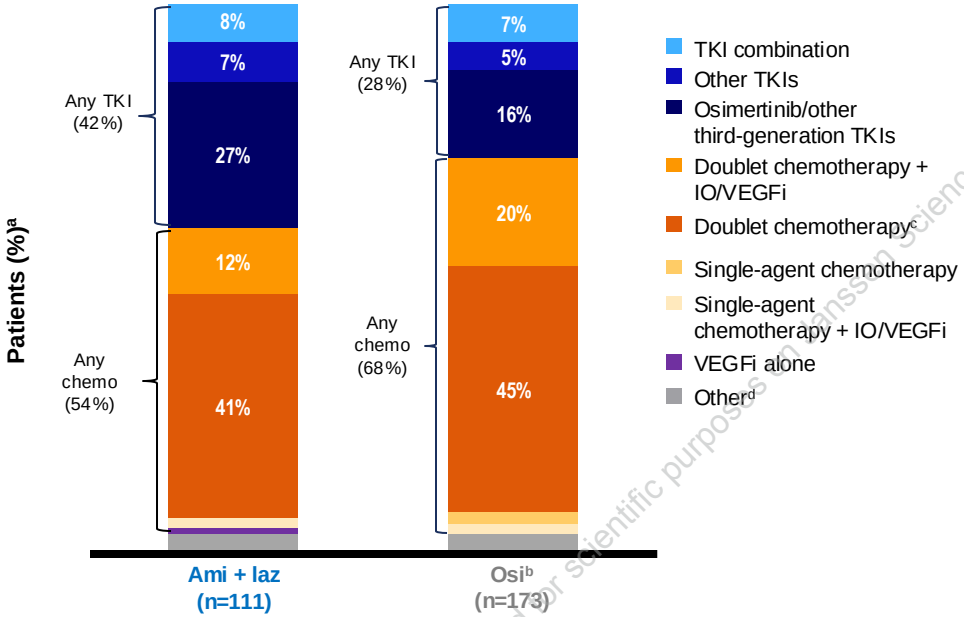
Amivantamab + lazertinib had significantly longer TTST



Fewer patients at the 3-year landmark on the amivantamab + lazertinib arm started a subsequent therapy versus osimertinib (45% vs 32%)

[a]TTST was defined as the time from the date of randomization to the start date of the subsequent anticancer therapy following study treatment discontinuation or death, whichever came first.[b]*P*-value was calculated from a log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified proportional hazards model.

First Subsequent Therapy



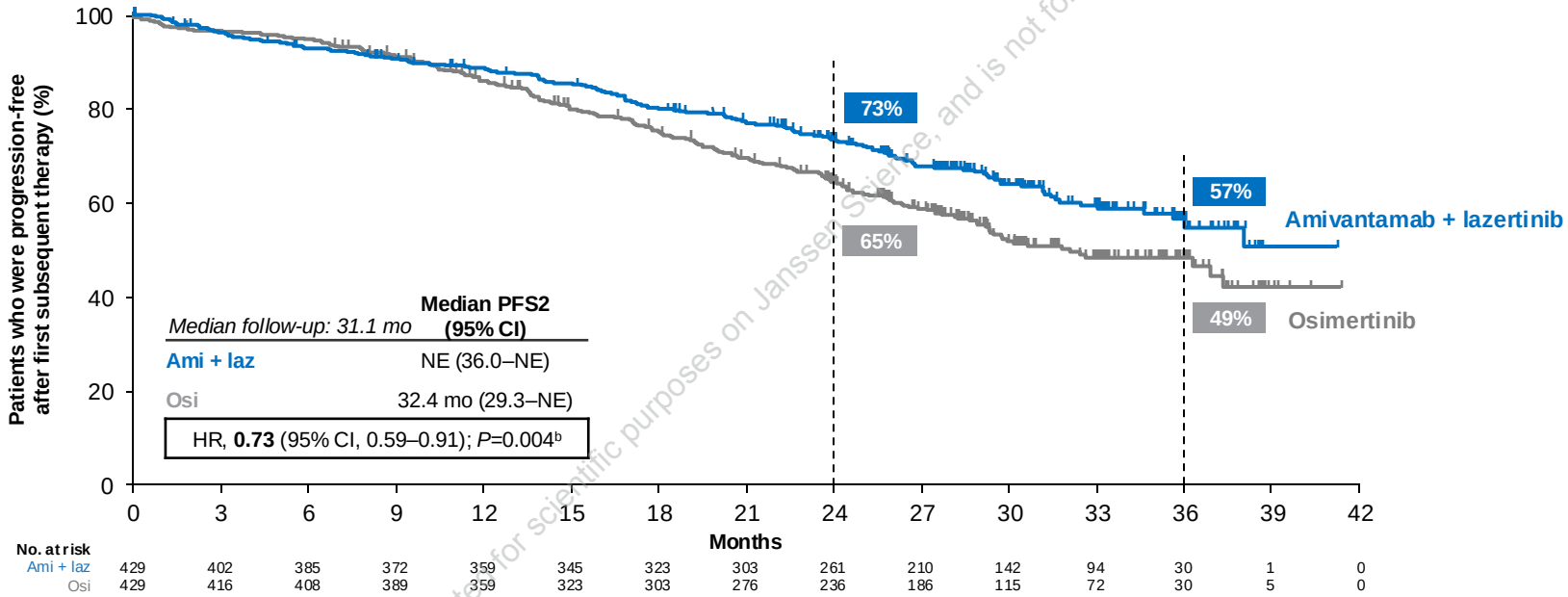
The proportion of patients that progressed, discontinued treatment, and went on to receive subsequent therapy was similar between arms (amivantamab + lazertinib: 72% vs osimertinib: 74%)[e]

The majority of patients who discontinued study treatment received 2L therapy, with chemotherapy being the most common subsequent therapy class in both arms

[a]Percentages may not sum to 100 due to rounding. [b]Two patients in the osimertinib arm received amivantamab as a subsequent treatment (one as a monotherapy and one in combination with lazertinib). [c]Includes one patient who received herbal + doublet chemotherapy. [d]Other category included herbals, ADCs, ALK TKIs, C-MET TKIs, amivantamab, and investigational agents. [e]Among patients with progressive disease who discontinued treatment.

PFS2: PFS After First Subsequent Therapy[a]

Amivantamab + lazertinib significantly reduced the risk of 2nd disease progression or death by 27%

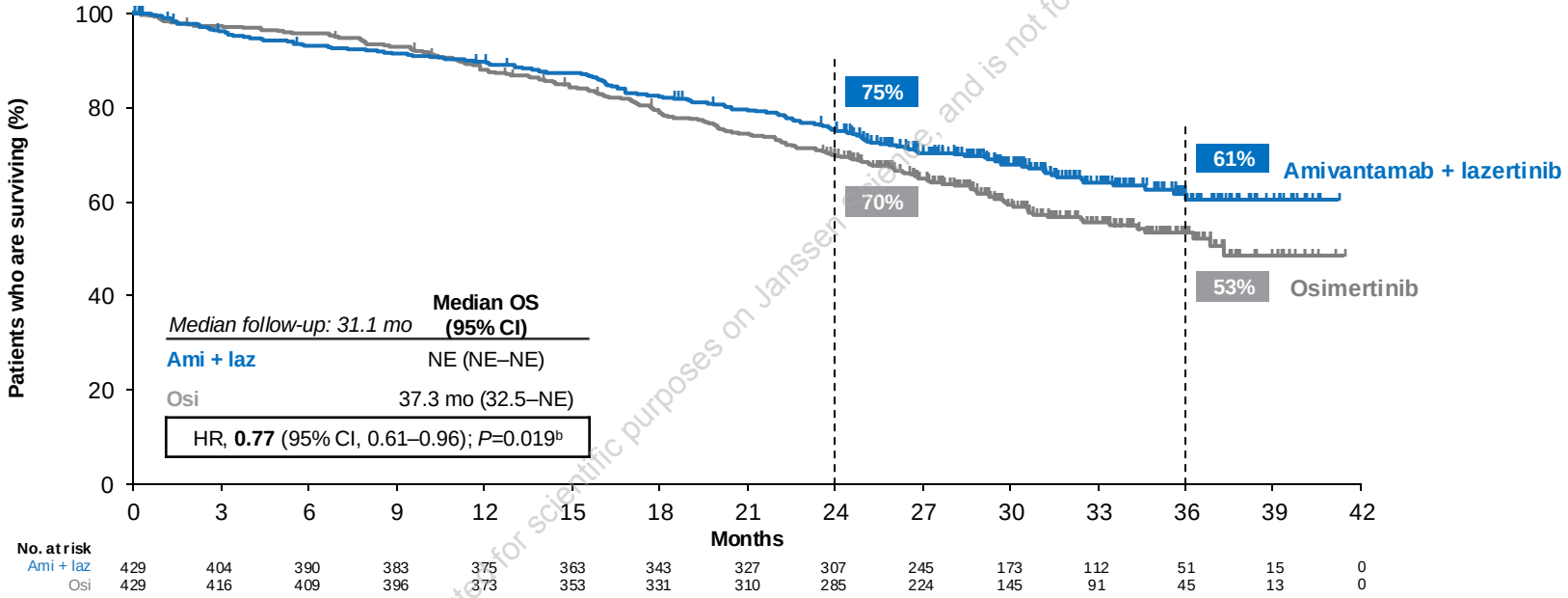


3-year landmark PFS2 was 57% for amivantamab + lazertinib vs 49% for osimertinib

[a]PFS2 was defined as the time from randomization until the date of second objective disease progression after initiation of subsequent anticancer therapy, based on clinical progression as determined by the investigator or death, whichever occurred first. [b]*P*-value is calculated by log-rank test stratified by mutation type (Ex19del or L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent).Hazard ratio was calculated from a stratified proportional hazards model.

Updated Overall Survival Analysis[a]

A strong OS trend favoring amivantamab + lazertinib was observed



OS curves separate early and widen over time favoring amivantamab + lazertinib, with 61% of patients alive at 3 years vs 53% with osimertinib

[a]This analysis was requested by health authorities and had nominal alpha spend. A *P*-value of ≤0.00001 was required for statistical significance. [b]P-value was calculated from a log-rank test stratified by mutation type (Ex19del or Exon 21 L858R), race (Asian or Non-Asian), and history of brain metastasis (present or absent). Hazard ratio was calculated from a stratified proportional hazards model.

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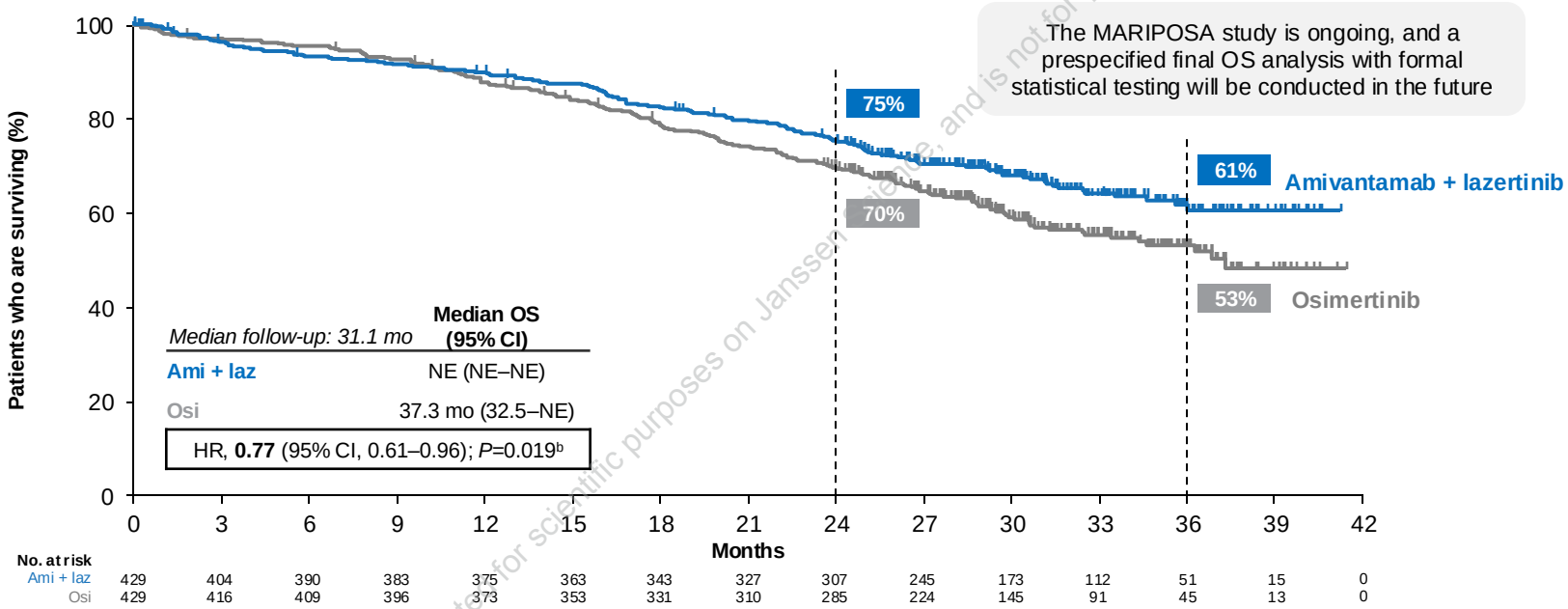

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Conclusion

- After longer follow-up (median: 31.1 months), data continue to favor first-line amivantamab + lazertinib over osimertinib with a promising OS trend (HR, 0.77; *P*=0.019[a]) 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
- First-line amivantamab + lazertinib showed reduced risk of CNS progression and sustained CNS control with more durable responses
  - 3-year intracranial PFS was double for amivantamab + lazertinib vs osimertinib (38% vs 18%)
  - Amivantamab + lazertinib showed a favorable trend for intracranial DoR (NE vs 24.4 months)
- Post-progression outcomes (TTD, TTST, PFS2) were significantly improved with first-line amivantamab + lazertinib vs osimertinib

Amivantamab + lazertinib is FDA approved for first-line *EGFR*-mutant NSCLC and is improving long-term outcomes vs osimertinib, based on its multitargeted mechanism and blocking of EGFR and MET with immune cell–directing activity

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

[a]This analysis was requested by health authorities and had nominal alpha spend. A *P*-value of ≤0.00001 was required for statistical significance.

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COCOON Trial Aims to Reduce Dermatologic Adverse Events Associated With 1L Amivantamab + Lazertinib

Key eligibility criteria

- Locally advanced or metastatic NSCLC
- Treatment-naïve for advanced disease
- Documented *EGFR* Ex19del or L858R
- ECOG PS score of 0 or 1

Stratification factors

- Race (Asian vs non-Asian)
- Age (<65 years vs ≥65 years)

IV amivantamab
1050 mg (1400 mg if ≥80 kg) once weekly for 4 weeks; every 2 weeks thereafter
+
Oral lazertinib
240 mg QD

1:1 randomization (N≈180[a]; US, EU, LATAM, APAC)

Arm A: amivantamab + lazertinib + enhanced dermatologic management (n=90)[b]

Prophylactic antibiotics

Weeks 1–12	Weeks 13–52
Chlorhexidine 4% on the fingernails and toenails QD	Topical clindamycin lotion 1% on scalp QD before bedtime

Paronychia prophylaxis
Chlorhexidine 4% on the fingernails and toenails QD

Skin moisturization
La Roche Posay Lipikar AP+M Moisturizer on the body and face at least QD

Arm B: amivantamab + lazertinib + standard dermatologic management (n=90)
Standard dermatologic management is based on the investigator and typically involves treatment

Primary Endpoint

- Incidence of grade ≥2 dermatologic AEs of interest in the first 12 weeks after initiation of amivantamab + lazertinib treatment in Arm A versus Arm B[c]

COCOON (ClinicalTrials.gov Identifier: NCT06120140).
[a]Planned enrollment is 180 patients, which is estimated to provide a power of 90%, with a 2-sided alpha of 0.05, to detect a treatment difference between Arms A and B in the incidence of grade ≥2 dermatologic AEs. [b]Enhanced dermatologic management was provided in addition to standard dermatologic management. [c]Dermatologic adverse events of interest included rash, dermatitis, paronychia, skin fissures, acne, erythema, skin exfoliation, skin lesion, skin irritation, and eczema.

Other Amivantamab Presentations at WCLC 2024

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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)

PALOMA-3

Subcutaneous vs intravenous amivantamab: patient satisfaction and resource utilization results

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

MARIPOSA

Lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 11:07-11:17am
(OA02.05; Lee)

SKIPPirr

Preventing infusion-related reactions with intravenous amivantamab: primary results

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

PAPILLON

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

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

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)

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- Medical writing assistance was provided by Lumanity Communications Inc., and funded by Janssen Global Services, LLC

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