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Effect of Amivantamab Dose Interruptions on Efficacy and Safety of First-line Amivantamab Plus Lazertinib in *EGFR*-mutant Advanced NSCLC: Exploratory Analyses From the MARIPOSA study

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Declaration of Interests

Maria del Rosario Garcia Campelo

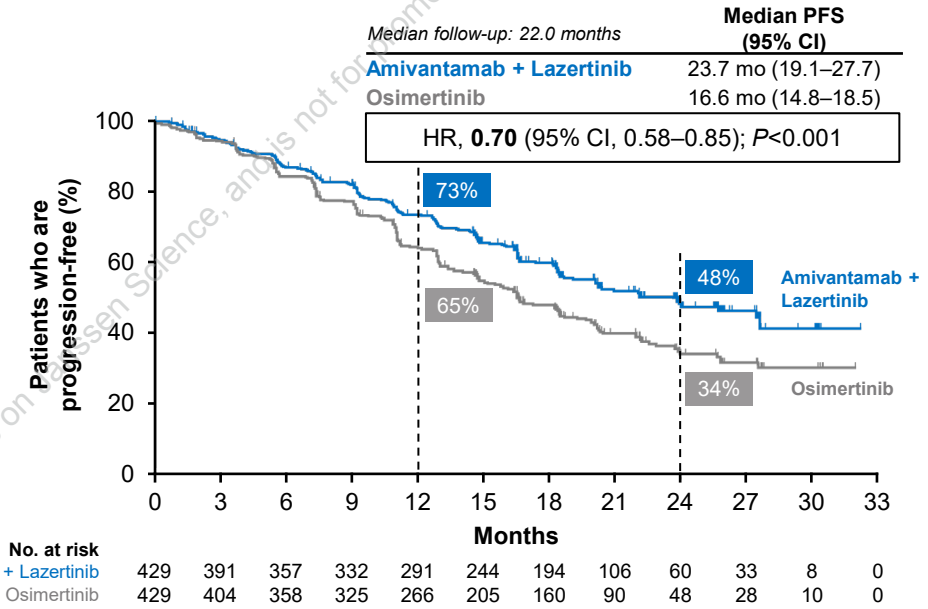
Consulting or advisory role: AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Janssen Oncology, MSD Oncology, Novartis, Pfizer, Roche/Genentech, and Takeda

Speakers bureau: Amgen, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Janssen Oncology, Eli Lilly, MSD Oncology, Novartis, Pfizer, Roche, Sanofi/Aventis, and Takeda

Travel, accommodations, expenses: MSD Oncology, Pfizer, and Roche/Genentech

Introduction

- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[1-3]
- Lazertinib is a CNS-penetrant, 3rd-generation EGFR TKI[4,5]
- In MARIPOSA, amivantamab + lazertinib significantly improved PFS vs osimertinib in treatment-naïve, *EGFR*-mutated, advanced NSCLC (Figure)[6]
  - Key AEs are highest in the **first 4 months**[7]
  - Protocol recommended amivantamab dose interruptions for grade ≥2 toxicities



We evaluated the association of amivantamab dose interruptions in the first 4 months with efficacy and safety outcomes of amivantamab + lazertinib

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

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Results: Descriptive Analysis of Amivantamab Dose Interruptions

- Among the 421 patients receiving ≥1 dose of amivantamab, 206 (49%) had a dose interruption within the first 4 months
- Dose interruption is defined as a skipped dose that is not made up; this population may also include patients that had a dose reduction or drug discontinuation
- Outcomes were similar among patients with and without dose interruptions (Table)

Endpoint, median (95% CI)	Dose interruptions in the first 4 months (n=206)	No interruptions in the first 4 months (n=215)	All randomized patients (n=429)
PFS	23.9 mo (18.5–NE)	23.7 mo (18.4–NE)	23.7 mo (19.1–27.7)
ORR	87% (81–91)	89% (84–93)	86% (83–89)
DoR among confirmed responders	25.8 mo (16.7–NE)	26.1 mo (20.1–NE)	25.8 mo (20.1–NE)

- However, this analysis measures exposure (interruptions) and outcomes over the same time period, which could lead to bias[a]

To minimize bias, we evaluated outcomes after the first 4 months (exposure period)[b]

[a]Outcomes, such as progression events or deaths, could occur before interruptions leading to outcomes-based selection bias.
[b]Patients who discontinued study, had disease progression, or died in the first 4 months were not evaluated, as they were not in the study by the cutoff timepoint (and the outcome event may occur prior to the interruption).

AE, adverse event; CI, confidence interval; DoR, duration of response; NE, not estimable; ORR, objective response date; PFS, progression-free survival.

Demographic and Baseline Characteristics

- 43/421 (10%) patients either discontinued study, had disease progression, or died prior to 4 months and are not included in this analysis[a]
- 188 patients had a dose interruption in the first 4 months and 190 did not
- Baseline characteristics were similar between patients with and without dose interruptions
- Among the 188 patients with dose interruptions:
  - Median time to first interruption: 43 days (IQR, 16–72)
  - Among the 94% who resumed amivantamab, the median interruption duration: 22 days (IQR, 14–41)

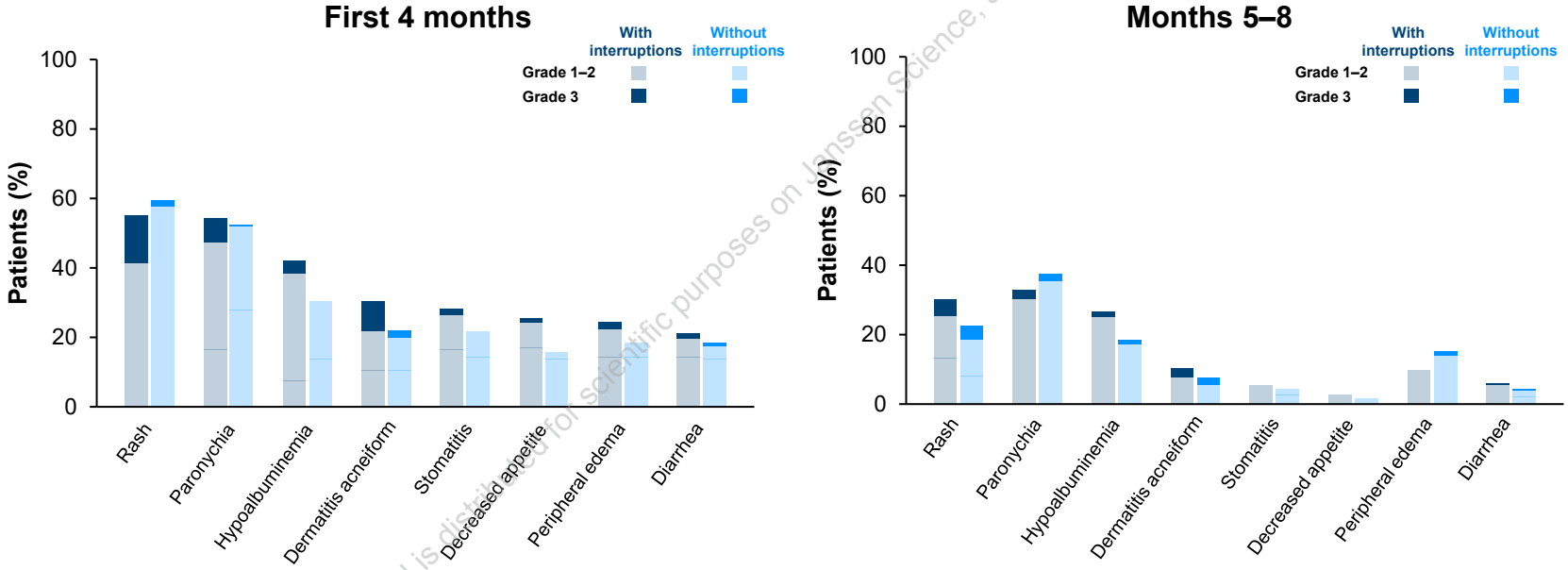
Characteristic, n (%)	Dose interruptions in the first 4 months (n=188)	No interruptions in the first 4 months (n=190)
Median age (range), years	63 (35–86)	62 (24–88)
Female	120 (64)	120 (63)
Race		
Asian	108 (57)	114 (60)
Non-Asian	78 (41)	76 (40)
Unknown	2 (1)	0
ECOG PS 1	122 (65)	127 (67)
History of smoking	61 (32)	54 (28)
History of brain metastases	80 (43)	71 (37)
EGFR mutation type		
Ex19del	101 (54)	124 (65)
L858R	87 (46)	66 (35)

[a]Removing patients who died, progressed, or discontinued within the first 4 months avoids outcome-based selection bias between dose interruption groups.

ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, Exon 19 deletion; IQR, interquartile range.

Prevalence and Severity of Key AEs Over Time

- Key AEs occurred most frequently during the first 4 months and declined over the next 4 months[a]
  - Notably, rash decreased by ~50%, paronychia by ~30%, and diarrhea by ~70%
- No grade 4 or 5 AEs were reported

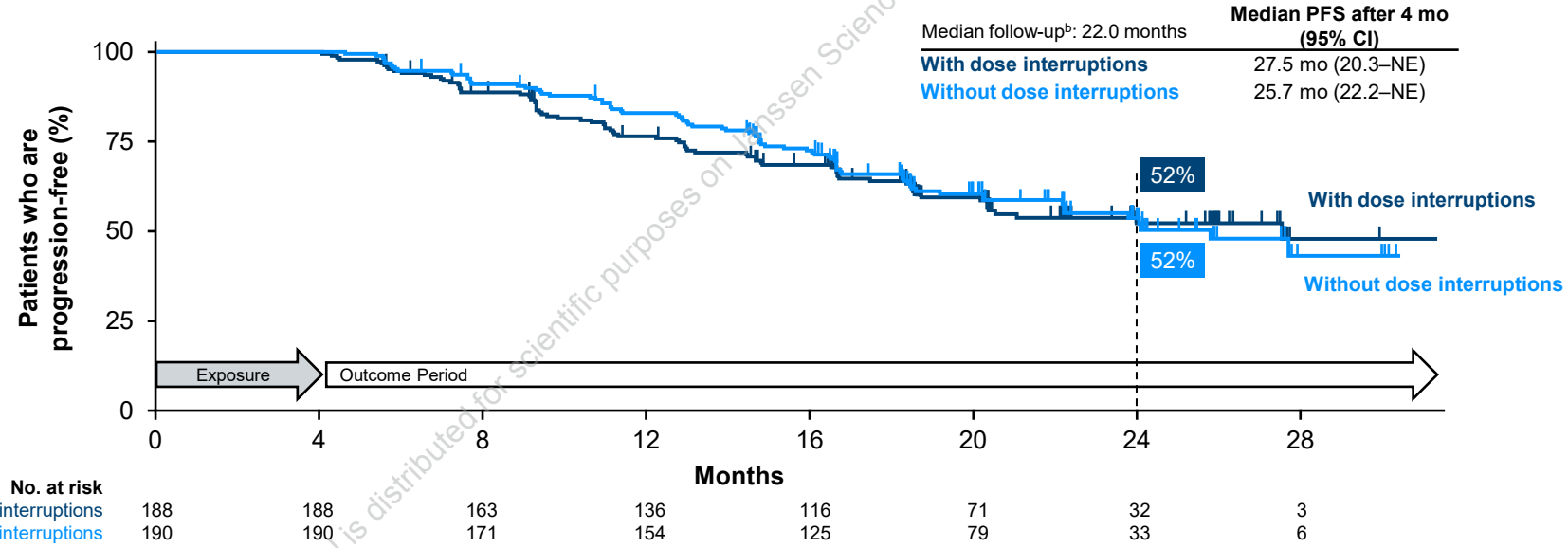


Note: The event experienced by the patient with the highest toxicity grade is reported. AEs are coded using MedDRA v25.0.

[a]Percent decrease in events during Months 5-8 relative to first 4 months: rash 46-63%; paronychia 29-39%; hypoalbuminemia 36-39%; dermatitis acneiform ~65%; stomatitis ~80%; decreased appetite ~89%; peripheral edema 17-60%; diarrhea 72-77%. AE, adverse event; MedDRA v25.0, Medical Dictionary for Regulatory Activities version 25.0.

Association of Dose Interruptions With Progression-Free Survival

- Median PFS after 4 months was similar between patients with and without dose interruptions
- The PFS HR by multivariable analysis[a] adjusting for age, ECOG PS, *EGFR* mutation type, Asian race, and history of brain metastases was **1.06** (95% CI, 0.73–1.44), indicating no significant association of dose interruption with PFS after the 4-month exposure period



[a]Via multivariate Cox proportional hazards model, only including patients still at risk of PFS at 4 months. [b]Median follow-up of the MARIPOSA study, as of the clinical cutoff of 11 August 2023, was 22.0 months.

CI, confidence interval; EGFR, epidermal growth factor receptor; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; NE, not estimable; PFS, progression-free survival.

Conclusions

- Approximately half of the patients treated with amivantamab + lazertinib required dose interruptions in the first 4 months
- Key skin and gastrointestinal AEs occurred early and diminished over time
  - No grade 4 or 5 AEs were reported
- Median PFS after 4 months was similar between patients with and without dose interruptions
- Dose interruptions are a meaningful way to manage AEs without compromising PFS

Amivantamab + lazertinib represents a new standard of care in patients with first-line, *EGFR*-mutant advanced NSCLC[1]

AE, adverse event; EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer; PFS, progression-free survival.

1. Cho BC, et al. Presented at: European Society for Medical Oncology (ESMO) Congress 2023; 20–24 October 2023; Madrid, Spain.

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