MARIPOSA-2

Amivantamab Plus Chemotherapy vs Chemotherapy in *EGFR*-mutant Advanced NSCLC After Progression on Osimertinib: Secondary Analyses of Patient-relevant Endpoints From MARIPOSA-2

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Background

- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[1-3]
- In MARIPOSA-2 (NCT04988295), amivantamab plus carboplatin-pemetrexed (chemotherapy) significantly prolonged PFS vs chemotherapy (HR, 0.48; *P*<0.001) in patients with osimertinib-pretreated, *EGFR*-mutant advanced NSCLC[4]
- Here, TTSP and patient-reported outcomes of amivantamab-chemotherapy vs chemotherapy from MARIPOSA-2 were evaluated

EGFR, epidermal growth factor receptor; HR, hazard ratio; NSCLC, non-small cell lung cancer; PFS, progression-free survival; TTSP, time to symptomatic progression.

1. Moores SL, et al. *Cancer Res.* 2016;76(13):3942-3953. 2. Vijayaraghavan S, et al. *Mol Cancer Ther.* 2020;19(10):2044-2056. 3. Yun J, et al. *Cancer Discov.* 2020;10(8):1194-1209. 4. Passaro A, et al. *Ann Oncol.* 2024;35(1):77-90.

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Phase 3 MARIPOSA-2 Study Design

Key eligibility criteria

- Locally advanced or metastatic NSCLC
- Documented *EGFR* Ex19del or L858R
- *Progressed on or after osimertinib monotherapy (as most recent line)*
- ECOG PS 0 or 1

2:2:1 randomization[a] (N=657)

Dosing schedule of the amivantamab-lazertinib-chemotherapy arm was modified during the study.[b] Results will be reported after additional follow-up.

- **Amivantamab-Lazertinib-Chemotherapy (n=263)**
- **Chemotherapy (n=263)**
- **Amivantamab-Chemotherapy (n=131)**

Focus of this presentation

Dosing (in 21-day cycles)

Amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) every 3 weeks starting at week 7 (first day of cycle 3)

Lazertinib: 240 mg daily starting after completion of carboplatin[c]

Chemotherapy on the first day of each cycle:

- **Carboplatin:** AUC5 for the first 4 cycles
- **Pemetrexed:** 500 mg/m^2 until disease progression

Dual primary endpoints of PFS by BICR according to RECIST v1.1:

- Amivantamab-Lazertinib-Chemotherapy vs Chemotherapy
- Amivantamab-Chemotherapy vs Chemotherapy

Secondary endpoints reported here:

- Time to symptomatic progression (TTSP)[c]
- Patient-reported outcomes by:
  - EORTC-QLQ-C30
  - PROMIS-PF 8c
  - NSCLC-SAQ

- MARIPOSA-2 is a global, randomized, phase 3 trial that compared amivantamab-chemotherapy and amivantamab-lazertinib-chemotherapy vs chemotherapy
- Secondary endpoints reported here include TTSP and PROs measured using the EORTC-QLQ-C30, NSCLC-SAQ, and PROMIS-PF 8c instruments
  - TTSP: time from randomization to onset of new/worsening symptoms related to lung cancer (per investigator) and required either a change in treatment and/or clinical intervention, or death

[a]Analyses were further stratified based on osimertinib line of therapy, history of brain metastases, and race (Asian vs non-Asian). [b]All patients randomized before 7-Nov-2022, initiated lazertinib on the first day of cycle 1. [c]Also included death

AUC, area under the curve; BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; Ex19del, Exon 19 deletion mutation; NSCLC, non-small cell lung cancer; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; PFS, progression-free survival; PROMIS-PF 8c, Patient-Reported Outcomes Measurement Information System Short Form v2.0–Physical Function 8c; RECIST, Response Evaluation Criteria in Solid Tumors.

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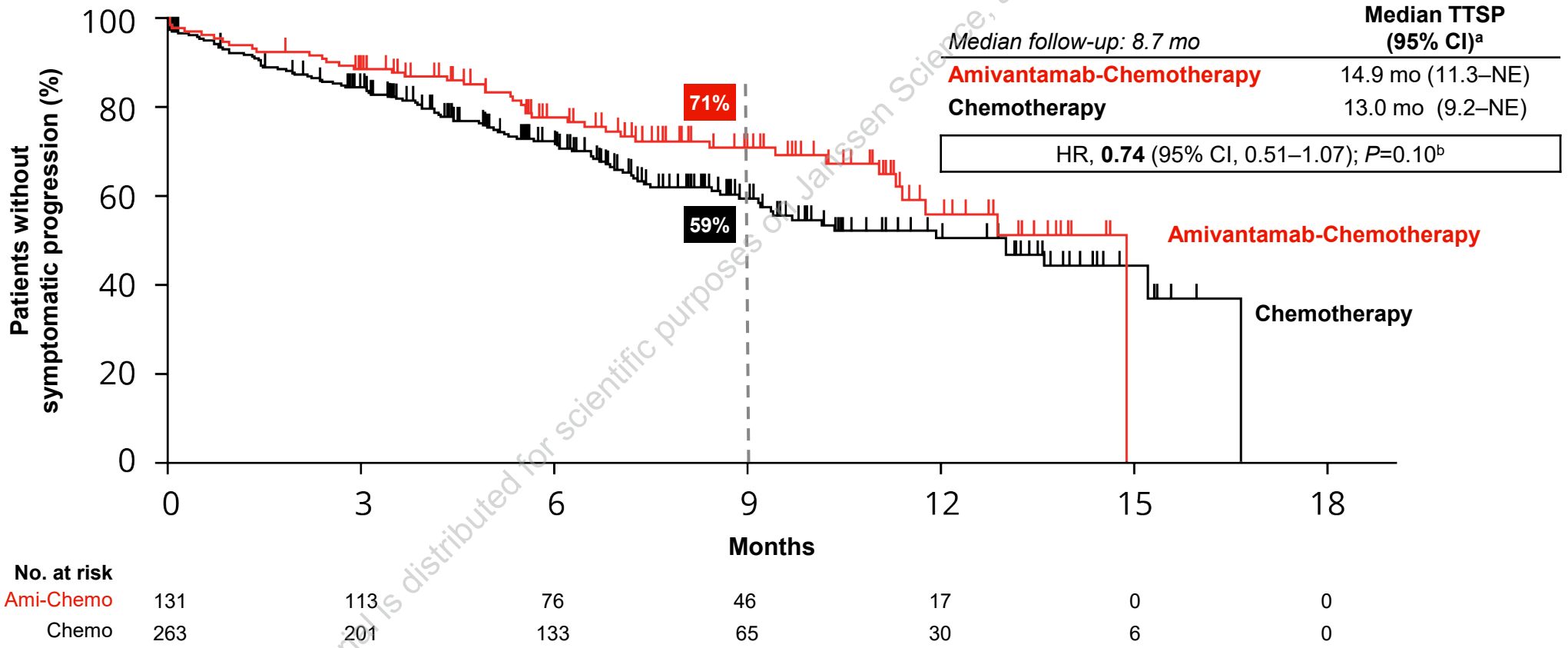
Time to Symptomatic Progression (TTSP)

- Amivantamab-chemotherapy reduced the risk of symptomatic progression by 26%



[a]Median TTSP of the ITT population with 95% CIs calculated using the Kaplan-Meier method. [b]HR with 95% CI calculated using a stratified Cox regression model; *P* value calculated using a stratified log-rank test.
Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not estimable; TTSP, time to symptomatic progression.

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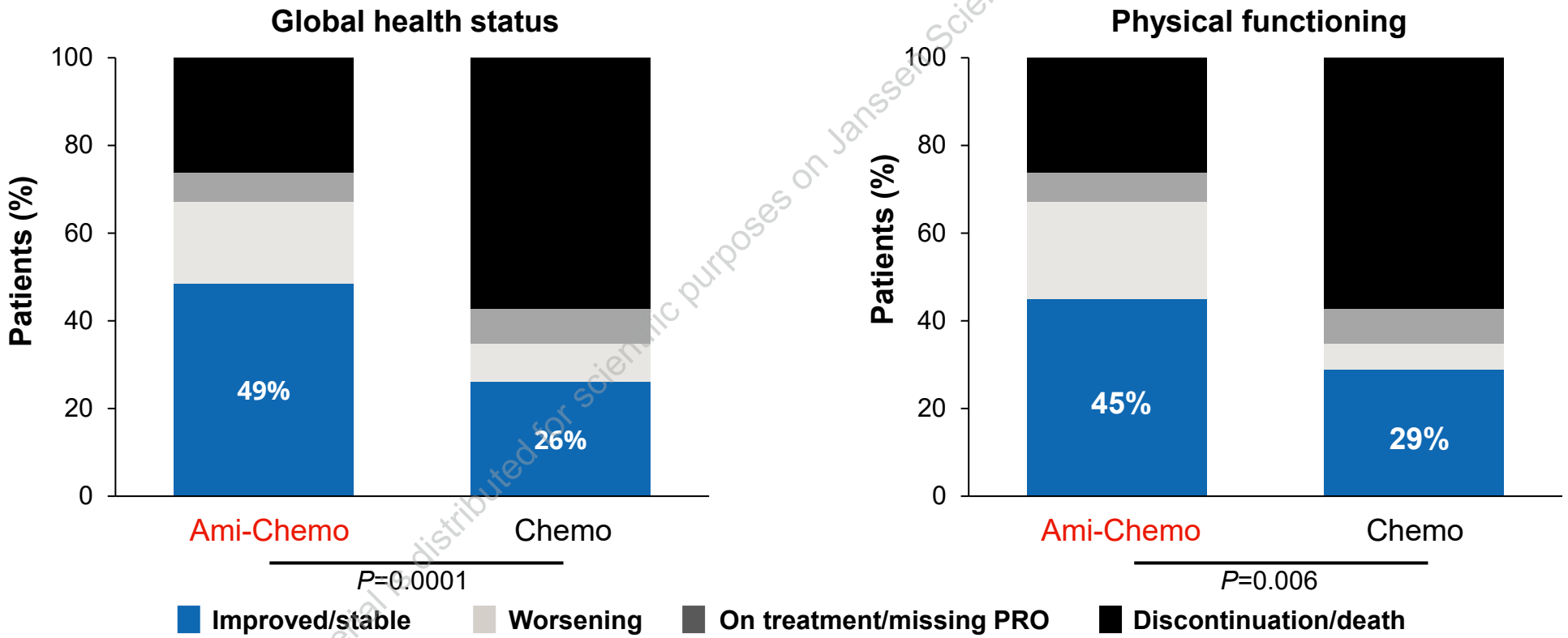
Patients Reporting Improved/Stable Symptoms at 6 Months by EORTC-QLQ-C30

- More patients in the amivantamab-chemotherapy arm reported improved or stable global health status and physical functioning vs chemotherapy at 6 months
  - Results were consistent for role, emotional, cognitive, and social functioning (all *P*<0.05)



Note: percentages exclude patients with insufficient follow-up. Role functioning is measured by limitation in pursuing work or other daily activities.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; EORTC-QLQ-C30, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire; PRO, patient-reported outcome.

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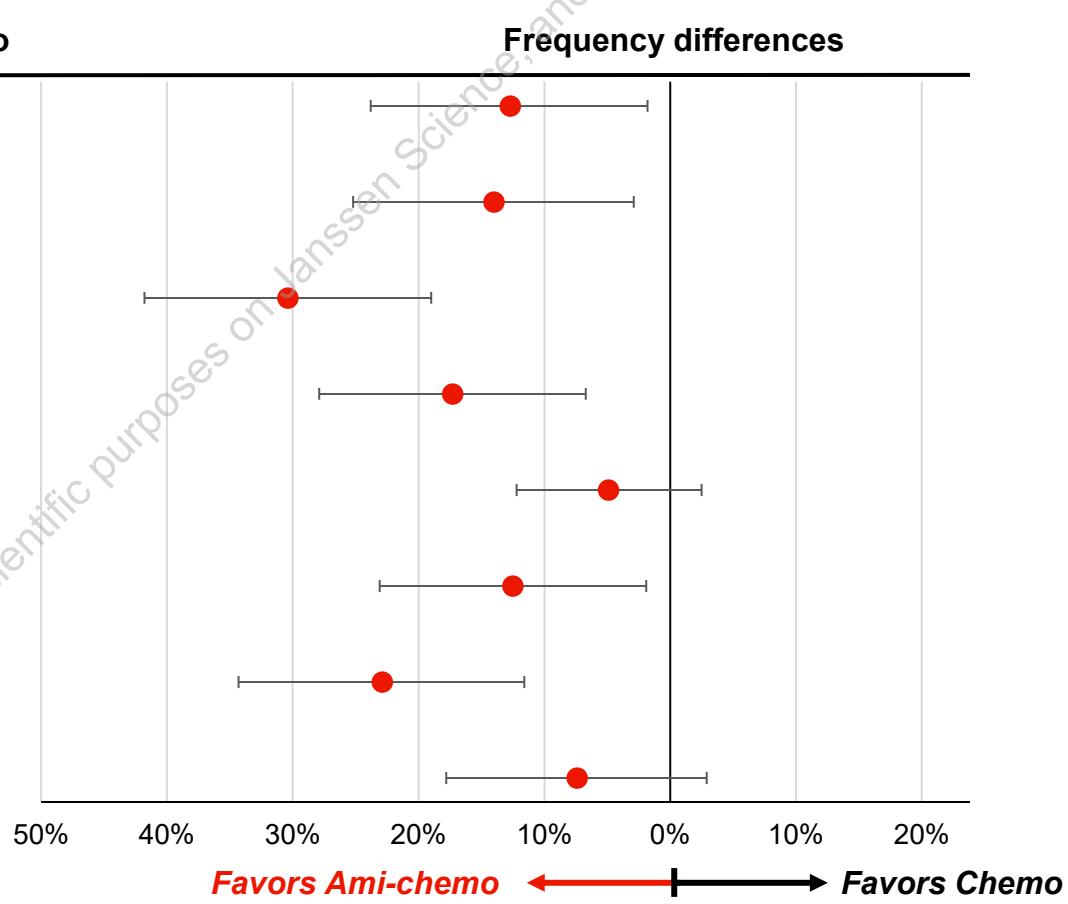
Patients Reporting Absence of Key Symptoms at 6 Months by EORTC-QLQ-C30

- More patients in the amivantamab-chemotherapy arm reported absence of key symptoms vs chemotherapy

Symptoms	Ami-Chemo	Chemo
Appetite loss	36%	24%
Constipation	38%	24%
Diarrhea	60%	29%
Dyspnea	35%	18%
Fatigue	12%	8%
Insomnia	32%	20%
Nausea and vomiting	49%	26%
Pain	28%	21%



Ami-Chemo, Amivantamab-Chemotherapy; Chemo, chemotherapy; EORTC-QLQ-C30, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire.

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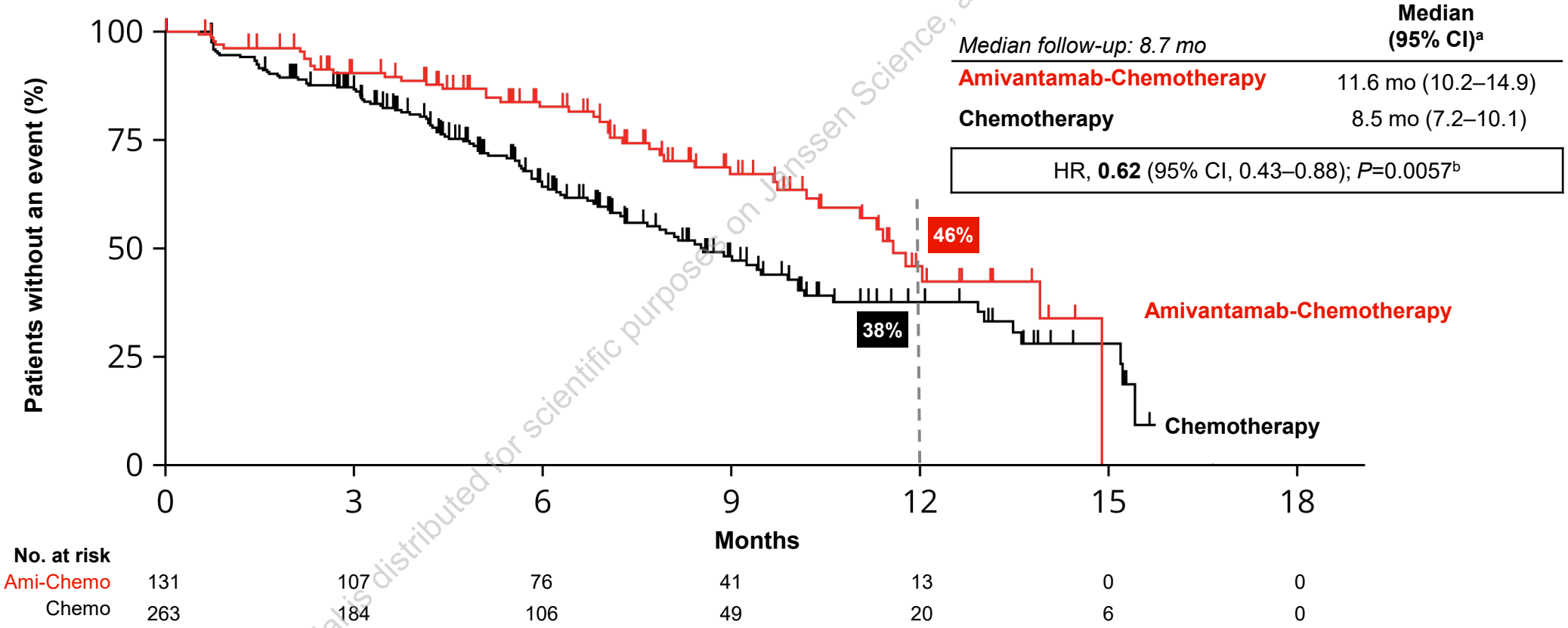
Time to Sustained Deterioration[a] in Total Symptom Score Over Time by NSCLC-SAQ

- Amivantamab-chemotherapy prolonged time to sustained deterioration in lung cancer symptoms vs chemotherapy



Median follow-up: 8.7 mo	Median (95% CI)[a]
Amivantamab-Chemotherapy	11.6 mo (10.2–14.9)
Chemotherapy	8.5 mo (7.2–10.1)

HR, **0.62** (95% CI, 0.43–0.88); *P*=0.0057[b]

[a]Time to sustained deterioration was defined as the time from randomization until the date of the first clinically meaningful deterioration (ie, decrease of ≥2.5 points relative to baseline) or death that was not subsequently followed by a score above the meaningful deterioration threshold at any later visits. [b]Kaplan-Meier analyses of PROs are influenced by disease progressions, which are not part of the definition, and patients post progression have fewer PRO data than those prior to progression.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; PRO, patient-reported outcome.

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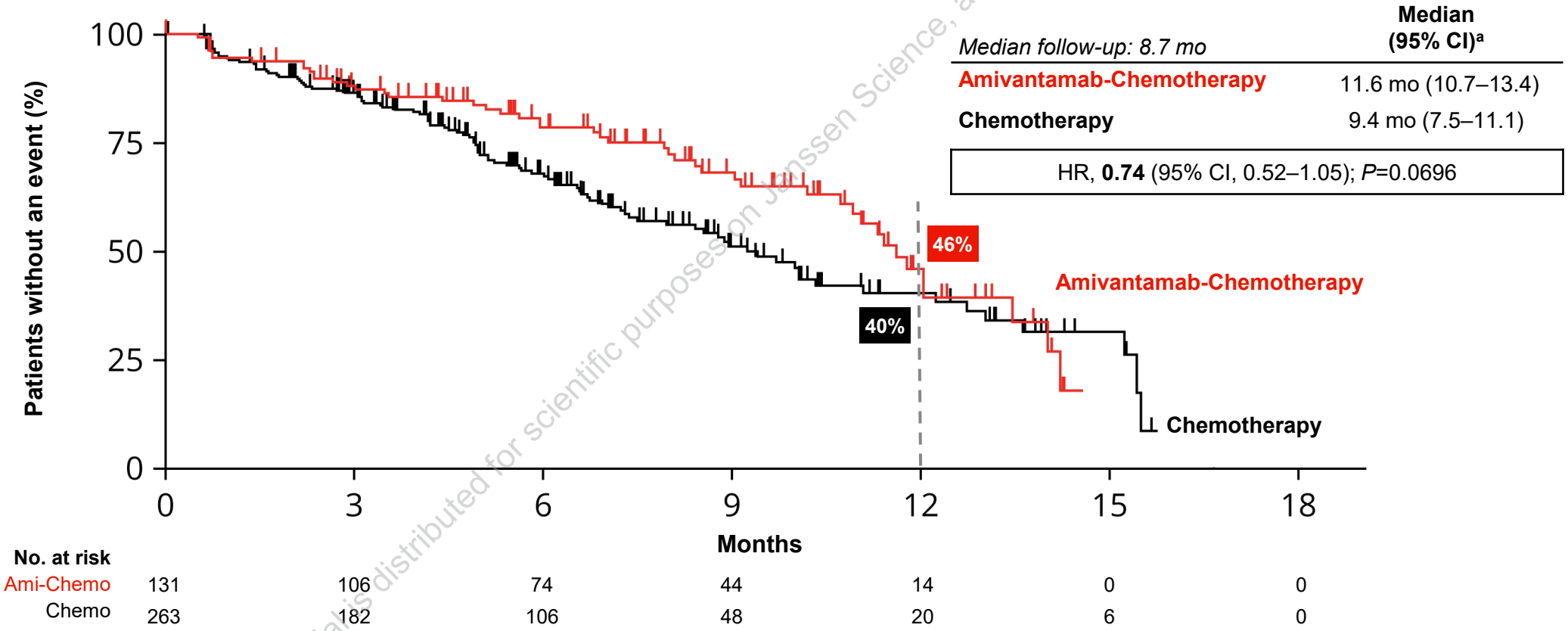
Time to Sustained Deterioration[a] in Physical Functioning Over Time by PROMIS-PF 8c

- Amivantamab-chemotherapy prolonged time to sustained deterioration in physical functioning vs chemotherapy



Median follow-up: 8.7 mo	Median (95% CI)[a]
Amivantamab-Chemotherapy	11.6 mo (10.7–13.4)
Chemotherapy	9.4 mo (7.5–11.1)

HR, **0.74** (95% CI, 0.52–1.05); *P*=0.0696

[a]Time to sustained deterioration was defined as the time from randomization until the date of the first clinically meaningful deterioration (ie, decrease of ≥6.5 points relative to baseline) or death that was not subsequently followed by a score above the meaningful deterioration threshold at any later visits.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; PROMIS-PF 8c, Patient-Reported Outcomes Measurement Information System Short Form v2.0–Physical Function 8c.

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Conclusions

- Amivantamab-chemotherapy numerically prolonged time to symptomatic progression vs chemotherapy (14.9 vs 13.0 mo; HR, 0.74; *P*=0.10)
- More patients in the amivantamab-chemotherapy arm reported improved/stable functioning and absence of key symptoms vs chemotherapy based on the EORTC-QLQ-C30
- Amivantamab-chemotherapy substantially prolonged time to sustained deterioration in lung cancer symptoms vs chemotherapy (11.6 vs 8.5 mo) based on the NSCLC-SAQ
- Amivantamab-chemotherapy numerically prolonged time to sustained deterioration in physical functioning vs chemotherapy (11.6 vs 9.4 mo) based on the PROMIS-PF 8c

CI, confidence interval; EORTC-QLQ-C30, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire; HR, hazard ratio; mo, month; NSCLC-SAQ, Non-Small Cell Lung Cancer Symptom Assessment Questionnaire; PROMIS-PF 8c, Patient-reported Outcomes Measurement Information System Physical Functioning Short Form 8c.

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Key Takeaway

Amivantamab-chemotherapy demonstrated improvements in time to symptomatic progression and key patient-reported outcomes compared to chemotherapy among patients with *EGFR*-mutant advanced NSCLC after disease progression on osimertinib

EGFR, epidermal growth factor receptor; NSCLC, non-small cell lung cancer.

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