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First-Line Amivantamab-chemotherapy vs Chemotherapy in NSCLC With *EGFR* Exon 20 Insertions: Overall Survival From PAPILLON

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Disclosures

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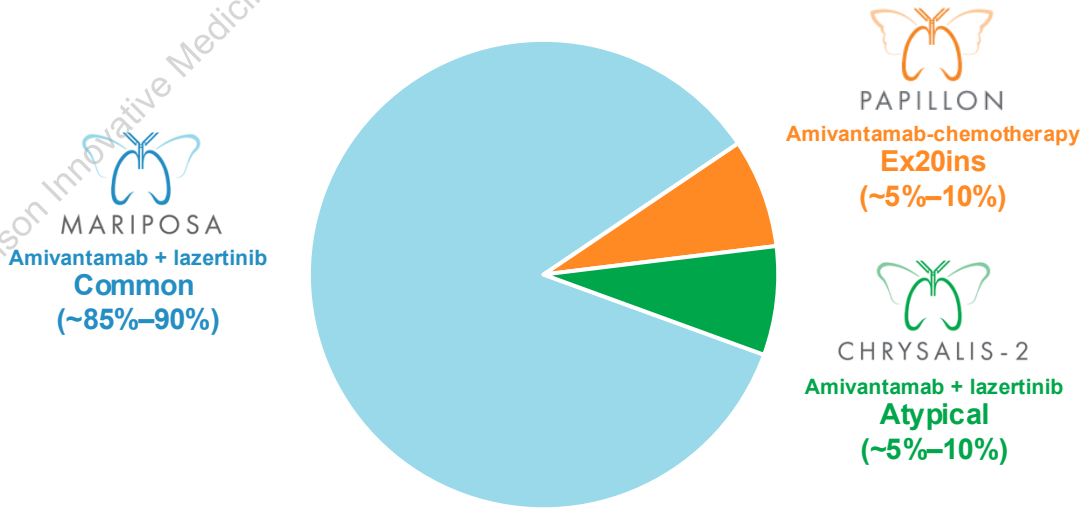
The authors report that generative AI was not used in the preparation of this presentation

PAPILLON
Ami-chemo in 1L
Ex20ins NSCLC

Background

- Amivantamab-based regimens have demonstrated durable benefit for patients with different types of *EGFR*-mutated NSCLC and other solid tumors[1–7]
- Prior to amivantamab, median real-world OS for *EGFR* Ex20ins NSCLC was approximately 16–24 months[8–10]
- PAPILLON met its primary endpoint demonstrating superior PFS (HR, 0.40; *P*<0.001) for amivantamab-chemotherapy over chemotherapy in treatment-naïve *EGFR* Ex20ins NSCLC[5]

Frequency of *EGFR* mutations evaluated in the amivantamab NSCLC clinical program[11–18,a]



Here, we report the protocol-specified final OS analysis for amivantamab-chemotherapy versus chemotherapy from PAPILLON

[a]Percentages do not sum to 100% due to variable ranges by sources. Ex20ins, exon 20 insertion.

1. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Janssen Biotech, Inc. 2025. 2. Yang JCH, et al. *N Engl J Med*. 2025;393(17):1681–1693. 3. Neal JW, et al. Presented at: American Society of Clinical Oncology (ASCO) Annual Meeting; May 29–June 2, 2026; Chicago, IL, USA. 4. Passaro A, et al. *Ann Oncol*. 2024;35(1):77–90. 5. Zhou C, et al. *N Engl J Med*. 2023;389(22):2039–2051. 6. Oberstein PE, et al. *J Clin Oncol*. 2026:44(17):1624–1634. 7. Burtness B, et al. *J Clin Oncol*. 2026;44(24):2271–2277. 8. SI Ou, et al. *JTO Clin Res Rep*. 2023;4(10):100558. 9. Bazhenova L, et al. *Lung Cancer*. 2021;162:154–161. 10. Chouaid C, et al. *Target Oncol*. 2021;16(6):801–811. 11. Riess JW, et al. *J Thorac Oncol*. 2018;13(10):1560–1568. 12. Gazdar AF. *Oncogene*. 2009;28(suppl 1):S24–S31. 13. Kobayashi S, et al. *J Thorac Oncol*. 2013;8(1):45–51. 14. Yang JCH, et al. *Lancet Oncol*. 2015;16(7):830–838. 15. Van Sanden S, et al. *Target Oncol*. 2022;17(2):153–166. 16. O'Kane GM, et al. *Lung Cancer*. 2017;109:137–144. 17. Vyse S, Huang PH. *Signal Transduct Target Ther*. 2019;4:5. 18. Attili I, et al. *Curr Oncol*. 2022;29(1):255–266.

PAPILLON: Phase 3 Study Design

Key eligibility criteria

- Treatment-naïve,[a] locally advanced or metastatic NSCLC
- Documented *EGFR* Ex20ins
- ECOG PS 0 or 1

Stratification factors

- ECOG PS
- History of brain metastases[b]
- Prior EGFR TKI use[a]

1:1 Randomization (N=308)

Amivantamab-chemotherapy (n=153)

Chemotherapy (n=155)

Crossover to 2L amivantamab monotherapy

- Crossover permitted only after BICR-confirmed disease progression
- Amivantamab monotherapy given Q3W

Primary endpoint: PFS by BICR according to RECIST v1.1[c]

Key secondary endpoint:

- Protocol-specified final overall survival (OS)[c]

Estimated to provide ~56% power to detect a statistically significant difference in OS, with statistical power further attenuated due to crossover

Other prespecified endpoints reported in this presentation:

- IPCW crossover-adjusted OS[d]
- PFS from randomization to second progression event (PFS2)
- Safety
- Patient-reported outcomes (PROs)

Dosing (in 21-day cycles)

Intravenous amivantamab: 1400 mg (1750 mg if ≥80 kg) for the first 4 weeks, then 1750 mg (2100 mg if ≥80 kg) Q3W starting at Week 7 (first day of Cycle 3)

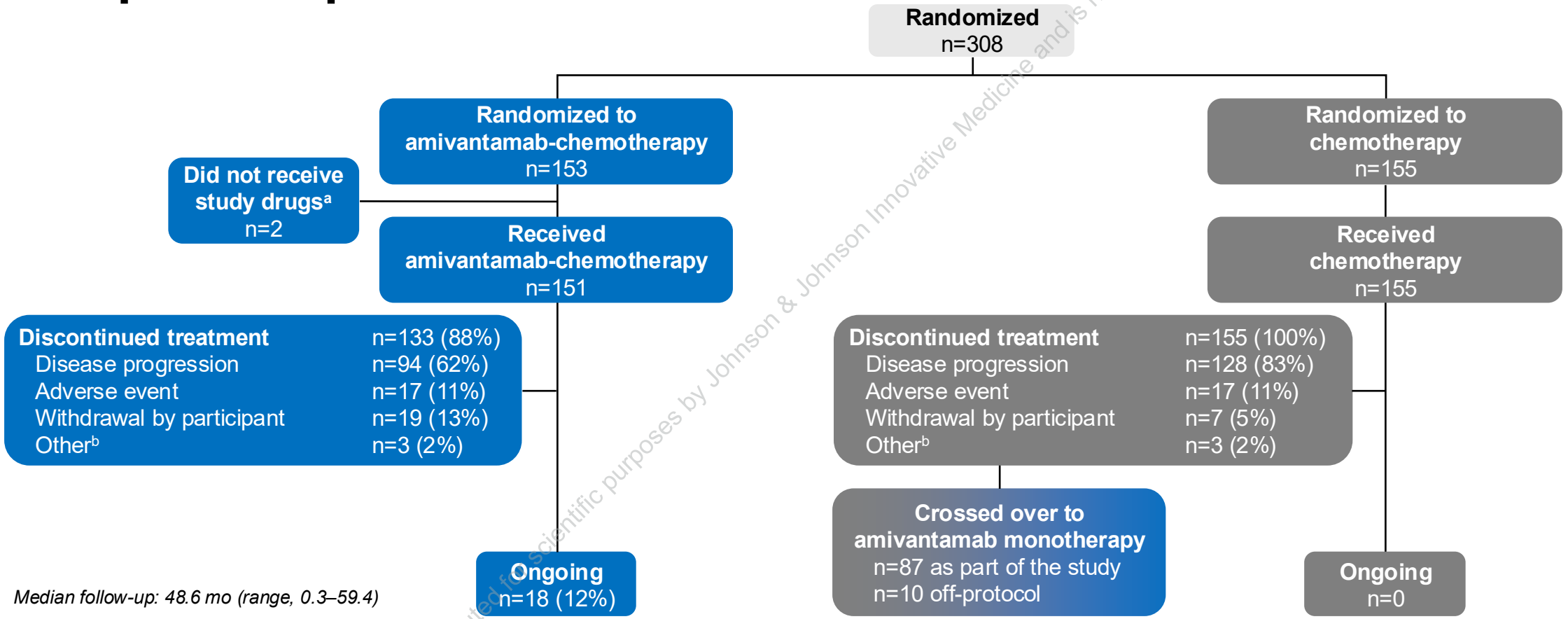
Chemotherapy on the first day of each cycle:

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

PAPILLON (ClinicalTrials.gov identifier: NCT04538664) enrollment period: December 2020 to November 2022; clinical cut-off: March 20, 2026.

[a]Removed as stratification factor since only 4 participants had prior EGFR TKI use (brief monotherapy with common EGFR TKIs was allowed if lack of response was documented). [b]Participants with brain metastases were eligible if they received definitive treatment and were asymptomatic, clinically stable, and off corticosteroid treatment for ≥2 weeks prior to randomization. [c]Key statistical assumption: 300 participants with 200 events needed for 90% power to detect an HR of 0.625 (estimated PFS of 8 vs 5 months). PFS, ORR, and then OS were included in hierarchical testing. [d]IPCW was a prespecified model for the crossover-adjusted OS analysis. 2L, second-line; AUC, area under the curve; Ex20ins, exon 20 insertion; IPCW, inverse probability of censoring weighting; RECIST, Response Evaluation Criteria in Solid Tumors.

Participant Disposition



Median follow-up: 48.6 mo (range, 0.3–59.4)

- The majority (76%; 97/128) crossed over to 2L amivantamab after discontinuing chemotherapy due to progressive disease

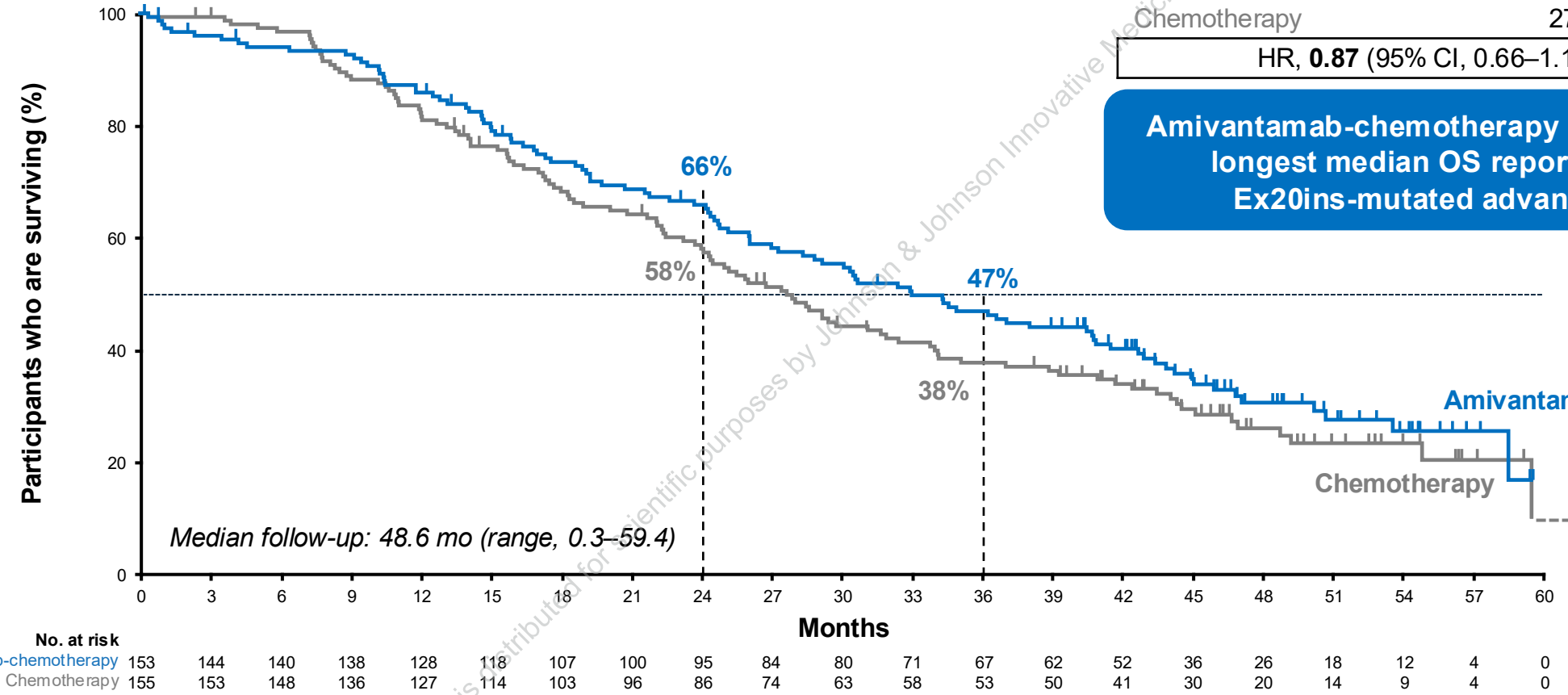
PAPILLON enrollment period: December 2020 to November 2022; clinical cut-off: March 20, 2026. [a]Both participants withdrew consent after randomization. [b]Other includes: noncompliance, other, and physician's decision (n≤2 for all). 2L, second-line.

PAPILLON: Final Overall Survival in the ITT Population

	Median OS (95% CI)
Amivantamab-chemotherapy	34.3 mo (27.0–40.8)
Chemotherapy	27.9 mo (24.0–32.4)

HR, **0.87** (95% CI, 0.66–1.14); *P*=0.307

Amivantamab-chemotherapy demonstrated the longest median OS reported to date in Ex20ins-mutated advanced NSCLC

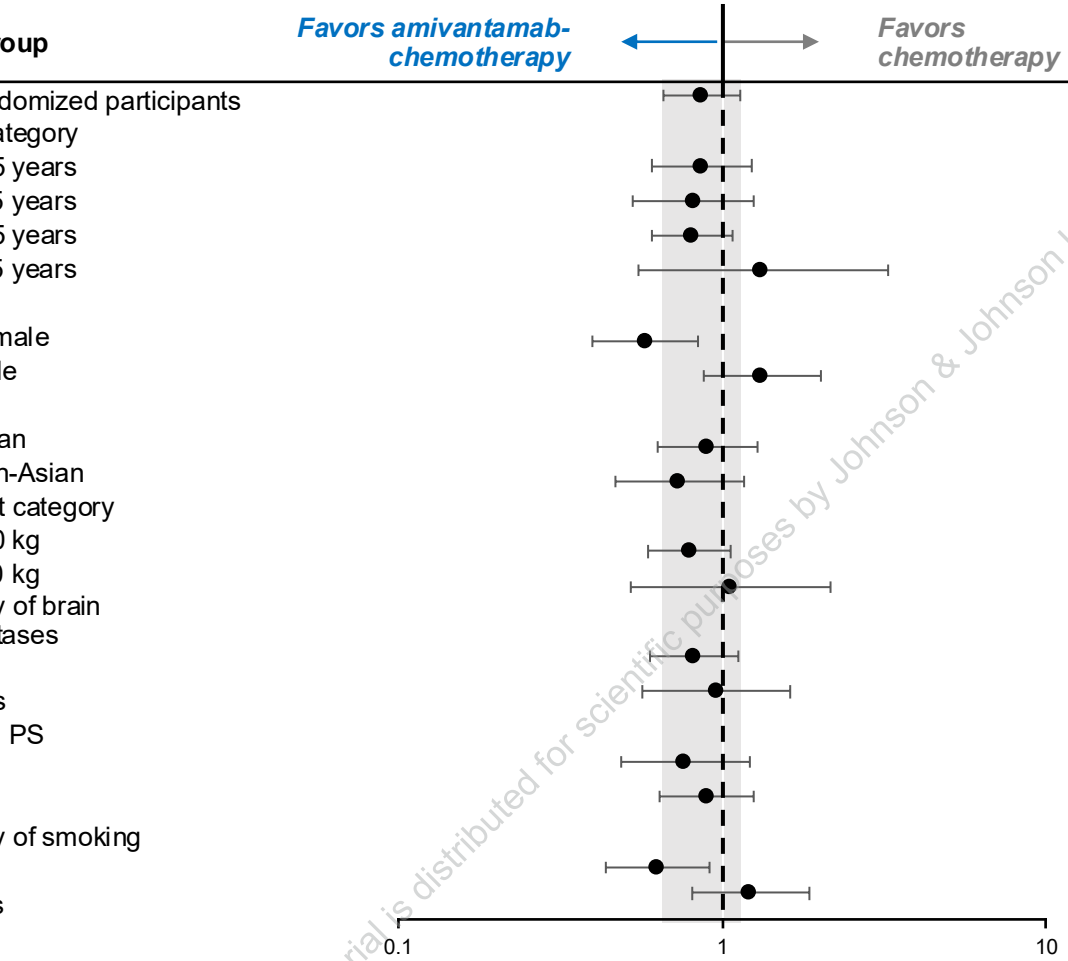


97 of 128 (76%) participants who discontinued due to progressive disease crossed over to amivantamab[a]

[a]A total of 97 participants (87 participants as part of the crossover cohort plus additional 10 participants off-protocol) received 2L amivantamab monotherapy out of 128 chemotherapy-randomized participants with BICR-confirmed disease progression. 2L, second-line; Ex20ins, exon 20 insertion.

Final Overall Survival in Predefined Subgroups

Across predefined subgroups, OS results generally favored amivantamab-chemotherapy



Subgroup	HR (95% CI)	N: Amivantamab-chemotherapy	N: Chemotherapy
All randomized participants	0.87 (0.66–1.14)	153	155
Age category			
<65 years	0.87 (0.61–1.24)	97	92
≥65 years	0.82 (0.53–1.26)	56	63
<75 years	0.81 (0.61–1.08)	141	140
≥75 years	1.33 (0.55–3.25)	12	15
Sex			
Female	0.58 (0.40–0.84)	85	93
Male	1.33 (0.88–2.01)	68	62
Race			
Asian	0.90 (0.63–1.28)	97	89
Non-Asian	0.74 (0.47–1.17)	53	62
Weight category			
<80 kg	0.80 (0.59–1.07)	132	128
≥80 kg	1.06 (0.52–2.16)	21	27
History of brain metastases			
No	0.82 (0.60–1.13)	117	117
Yes	0.97 (0.57–1.62)	36	38
ECOG PS			
0	0.77 (0.49–1.22)	59	58
1	0.90 (0.64–1.26)	94	97
History of smoking			
No	0.63 (0.44–0.91)	88	91
Yes	1.22 (0.81–1.85)	65	64

Note: Gray box indicates 95% CIs of HR for all randomized participants. Subgroup analyses were not part of the hypothesis testing of the trial and should not be used to infer definitive treatment effects.

PAPILLON: Crossover-Adjusted Final Overall Survival

Inverse Probability of Censoring Weighting (IPCW)

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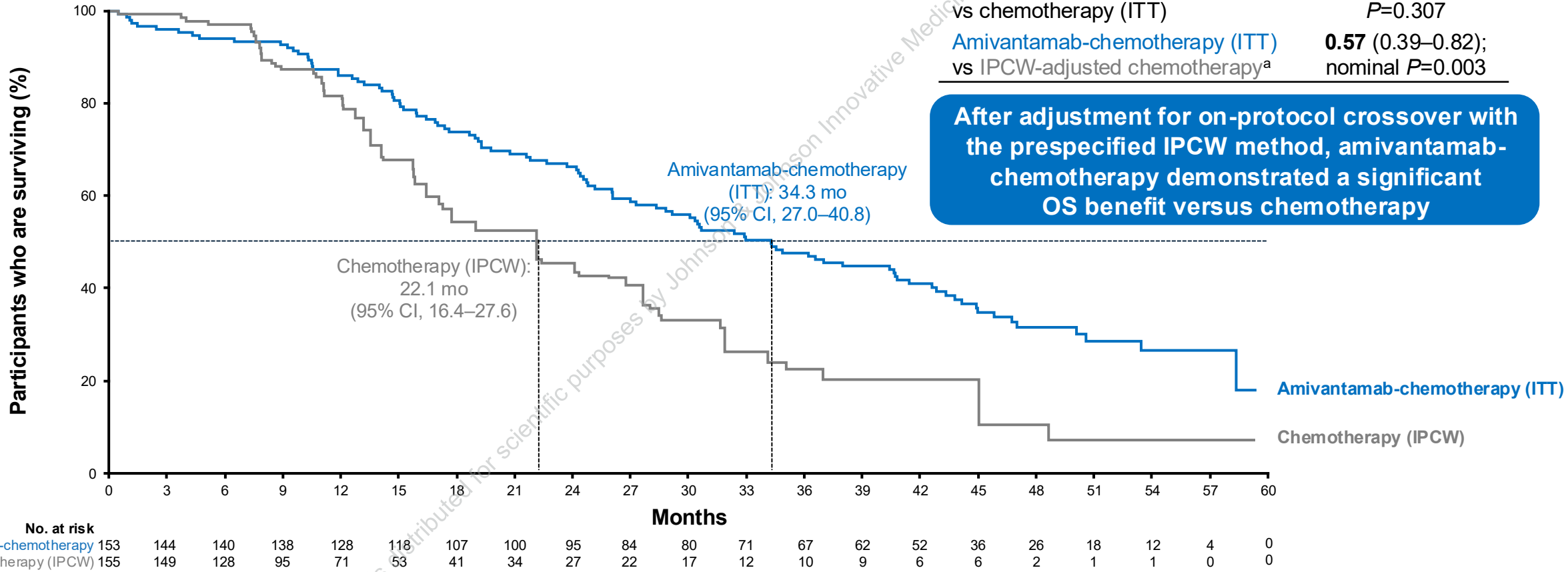
	HR (95% CI)
Amivantamab-chemotherapy (ITT) vs chemotherapy (ITT)	**0.87** (0.66–1.14); *P*=0.307
Amivantamab-chemotherapy (ITT) vs IPCW-adjusted chemotherapy[a]	**0.57** (0.39–0.82); nominal *P*=0.003

After adjustment for on-protocol crossover with the prespecified IPCW method, amivantamab-chemotherapy demonstrated a significant OS benefit versus chemotherapy



No. at risk																				
Amivantamab-chemotherapy	153	144	140	138	128	118	107	100	95	84	80	71	67	62	52	36	26	18	12	4	0
Chemotherapy (IPCW)	155	149	128	95	71	53	41	34	27	22	17	12	10	9	6	6	2	1	1	0	0

[a]Two additional recommended models[1] demonstrated improvement in the OS benefit consistent with IPCW: Two-Stage Estimation (TSE): HR, 0.54 (95% CI, 0.35–0.77) and Rank Preserving Structural Failure Time (RPSFT): HR, 0.71 (95% CI, 0.37–1.36).

1. Question and answer on adjustment for cross-over in estimating effects in oncology trials. European Medicines Agency. Accessed August 18, 2026. https://www.ema.europa.eu/en/documents/scientific-guideline/question-and-answer-adjustment-cross-over-estimating-effects-oncology-trials_en.pdf.

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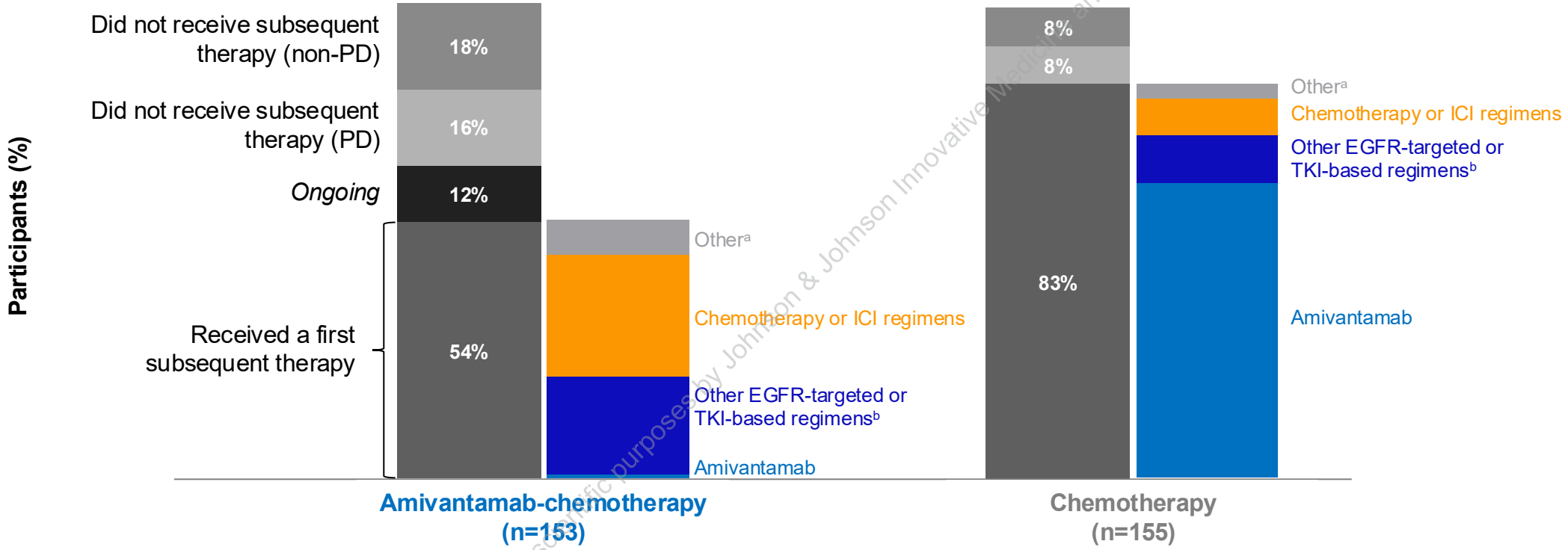
Ex20ins NSCLC

First Subsequent Therapy



- The crossover design for the chemotherapy arm and lack of active 2L therapies available at the time of this trial likely contributed to differences in rates between arms

Note: Totals may not sum to 100 due to rounding. 83 participants from the amivantamab-chemotherapy arm received a subsequent therapy (Amivantamab: n=2; Other EGFR-targeted or TKI-based regimens: n=31; Chemotherapy or ICI regimens: n=39; Other: n=11); 129 participants in the chemotherapy arm received a subsequent therapy (Amivantamab: n=97; Other EGFR-targeted or TKI-based regimens: n=15; Chemotherapy or ICI regimens: n=13; Other: n=4). [a]Other therapy included antineoplastic agents, bevacizumab, cantharidin, investigational agents, other protein kinase inhibitors, and SKB 264. [b]EGFR-targeted or TKI-based regimens included afatinib, firmonertinib, mobocertinib, ORIC 114, osimertinib, sunvozertinib, zipalertinib, and EGFR TKI combination regimens. TKI in combination with chemotherapy, immunotherapy, or VEGF inhibitor therapies were only counted in the TKI-based regimen category.

2L, second-line; ICI, immune checkpoint inhibitor; PD, progressive disease.

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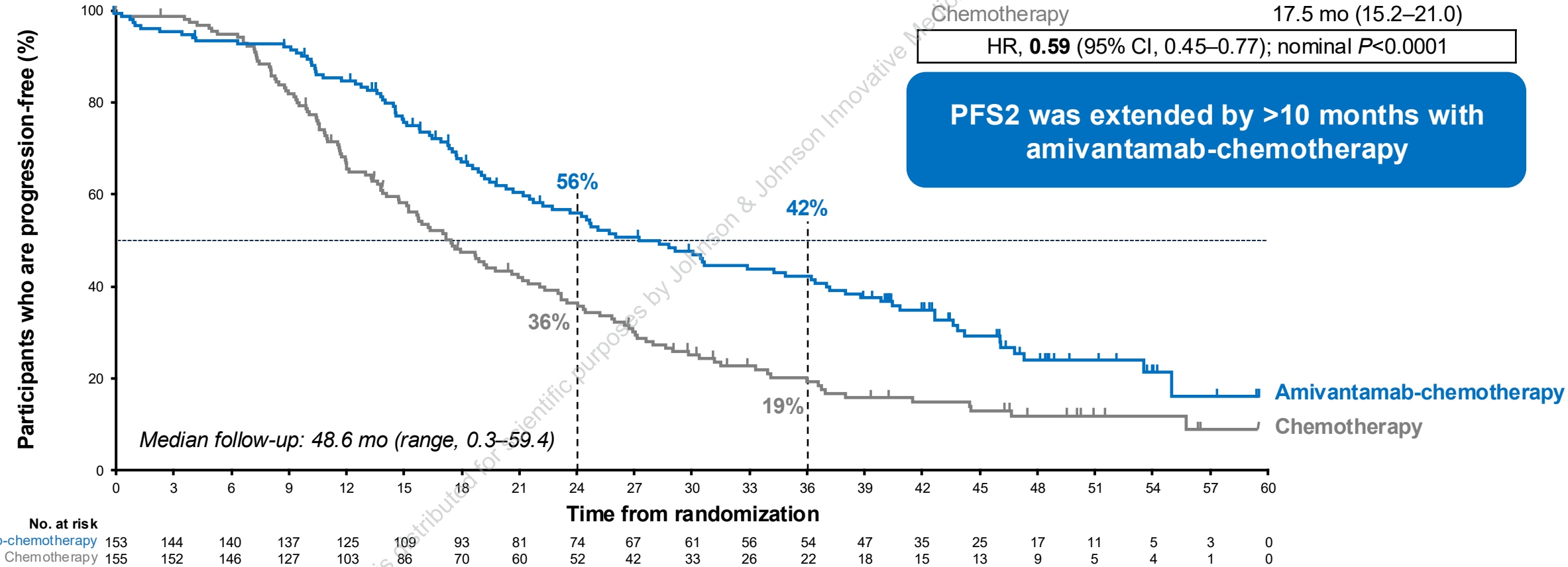
Ami-chemo in 1L Ex20ins NSCLC

PFS2: PFS From Randomization to Second Progression Event[a]

	Median PFS2 (95% CI)
Amivantamab-chemotherapy	28.3 mo (21.8–36.2)
Chemotherapy	17.5 mo (15.2–21.0)

HR, **0.59** (95% CI, 0.45–0.77); nominal *P*<0.0001

PFS2 was extended by >10 months with amivantamab-chemotherapy



[a]Consistent with PFS2, time to treatment discontinuation and time to subsequent therapy were extended with amivantamab-chemotherapy versus chemotherapy (14.1 vs 7.6 mo; HR, 0.36; 95% CI, 0.28–0.46; *P*<0.0001 and 16.9 vs 9.9 mo; HR, 0.37; 95% CI, 0.29–0.48; *P*<0.0001, respectively).

Safety

- The safety profile was consistent with prior reports, with no new safety signals identified[1,a]
- PAPILLON was conducted prior to evaluation of prophylactic strategies for AEs[2,3] and subcutaneous amivantamab[4,5]

Most common AEs of any cause by preferred term (≥30%), n (%)	Amivantamab-chemotherapy (n=151)		Chemotherapy (n=155)	
	All grades	Grade ≥3	All grades	Grade ≥3
Associated with EGFR inhibition				
Paronychia	91 (60)	15 (10)	0	0
Rash	88 (58)	22 (15)	13 (8)	0
Dermatitis acneiform	47 (31)	9 (6)	5 (3)	0
Associated with MET inhibition				
Hypoalbuminemia	70 (46)	8 (5)	15 (10)	0
Peripheral edema	52 (34)	4 (3)	18 (12)	0
Other				
Neutropenia	91 (60)	52 (34)	71 (46)	35 (23)
Anemia	80 (53)	19 (13)	87 (56)	20 (13)
Infusion-related reaction	66 (44)	2 (1)	2 (1)	0
Constipation	61 (40)	0	51 (33)	1 (1)
Nausea	60 (40)	2 (1)	67 (43)	0
Decreased appetite	60 (40)	5 (3)	46 (30)	2 (1)
Leukopenia	57 (38)	17 (11)	50 (32)	5 (3)
Thrombocytopenia	57 (38)	15 (10)	46 (30)	16 (10)
Alanine aminotransferase increased	56 (37)	9 (6)	57 (37)	2 (1)
Aspartate aminotransferase increased	54 (36)	3 (2)	53 (34)	1 (1)

Note: A total of 151 participants were included in the amivantamab-chemotherapy arm as part of the safety population, as 2 participants withdrew consent after randomization and did not receive study drugs. [a]Median treatment duration was 13.4 mo for amivantamab-chemotherapy and 6.9 mo for chemotherapy.

1. Zhou C, et al. *N Engl J Med*. 2023;389(22):2039–2051. 2. Spira AI, et al. *J Thorac Oncol*. 2025;20(6):809–816. 3. Cho BC, et al. *J Thorac Oncol*. 2025;20(10):1517–1530. 4. Alexander M, et al. *Eur J Cancer*. 2025;227:115624. 5. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use [package insert]. Janssen Biotech, Inc; 2026.

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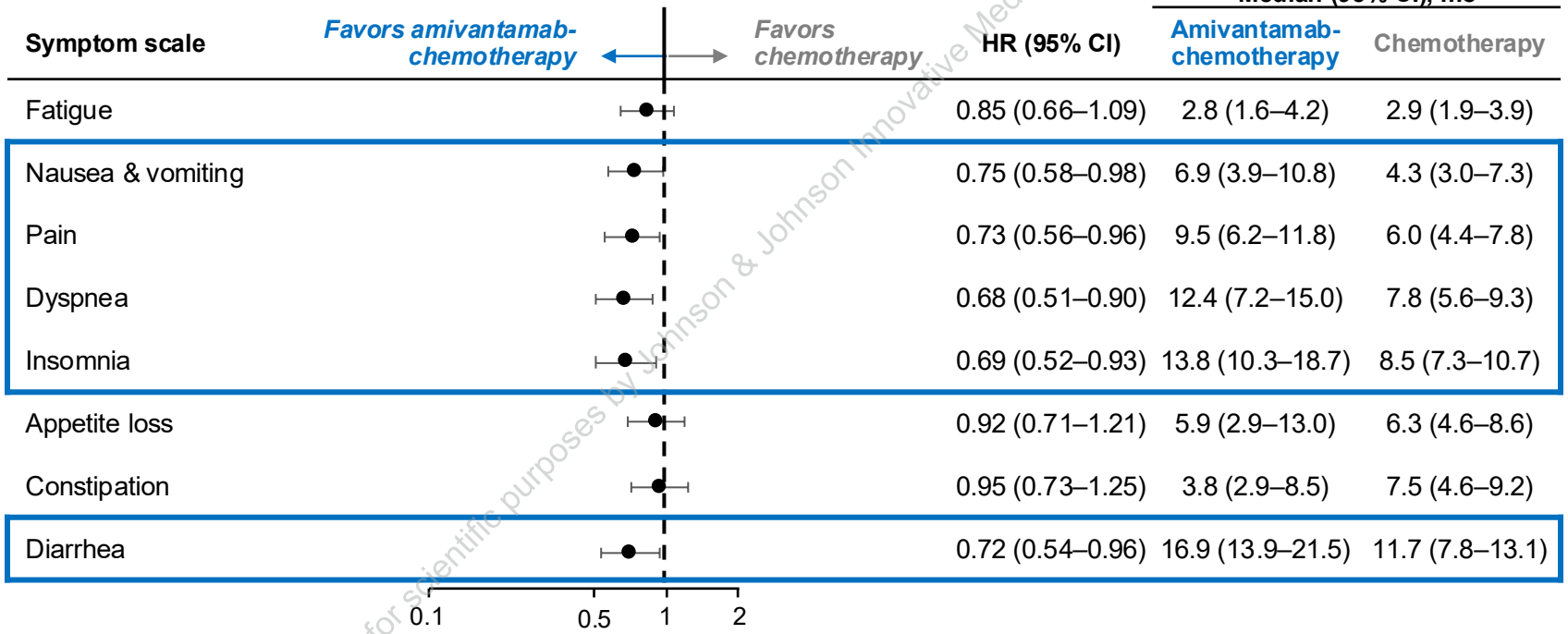
Amivantamab-chemotherapy prolonged time to worsening of symptoms versus chemotherapy[a]

Time to deterioration by EORTC QLQ-C30 symptom scales



Symptom scale	HR (95% CI)	Median (95% CI), mo: Amivantamab-chemotherapy	Median (95% CI), mo: Chemotherapy
Fatigue	0.85 (0.66–1.09)	2.8 (1.6–4.2)	2.9 (1.9–3.9)
Nausea & vomiting	0.75 (0.58–0.98)	6.9 (3.9–10.8)	4.3 (3.0–7.3)
Pain	0.73 (0.56–0.96)	9.5 (6.2–11.8)	6.0 (4.4–7.8)
Dyspnea	0.68 (0.51–0.90)	12.4 (7.2–15.0)	7.8 (5.6–9.3)
Insomnia	0.69 (0.52–0.93)	13.8 (10.3–18.7)	8.5 (7.3–10.7)
Appetite loss	0.92 (0.71–1.21)	5.9 (2.9–13.0)	6.3 (4.6–8.6)
Constipation	0.95 (0.73–1.25)	3.8 (2.9–8.5)	7.5 (4.6–9.2)
Diarrhea	0.72 (0.54–0.96)	16.9 (13.9–21.5)	11.7 (7.8–13.1)

- Aligned with the improved patient-reported outcomes, TTSP[b] was prolonged with amivantamab-chemotherapy versus chemotherapy (28.8 vs 22.4 mo; HR, 0.77; 95% CI, 0.59–1.01; *P*=0.055)

Note: Blue boxes indicate *P*<0.05. [a]Time to worsening in EORTC QLQ-C30 symptom scales was defined as the time from randomization until the first clinically meaningful worsening in the symptom (an increase of ≥10 points) or death.[1] [b]TTSP was defined as the time from randomization to the onset of new or worsening symptoms that was considered by the investigator to be related to lung cancer and required either a change in anticancer treatment and/or clinical intervention to manage symptoms, whichever occurred first. EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; TTSP, time to symptomatic progression. 1. Osoba D, et al. *J Clin Oncol*. 1998;16(1):139–144.

Conclusions

- With a median follow-up of >4 years, 1L amivantamab-chemotherapy demonstrated the longest median OS to date (34.3 months) in participants with *EGFR* Ex20ins advanced NSCLC (HR, 0.87)
- After adjusting for substantial on-protocol crossover to amivantamab in the chemotherapy arm, amivantamab-chemotherapy demonstrated a significant OS benefit (IPCW HR, 0.57; nominal *P*=0.003)
- The safety profile of amivantamab-chemotherapy was consistent with prior reports before subcutaneous amivantamab and prophylactic strategies,[1] with patient-reported outcomes favoring the amivantamab-chemotherapy arm

Amivantamab-chemotherapy demonstrated the longest median OS reported to date, supporting it as a foundational 1L regimen

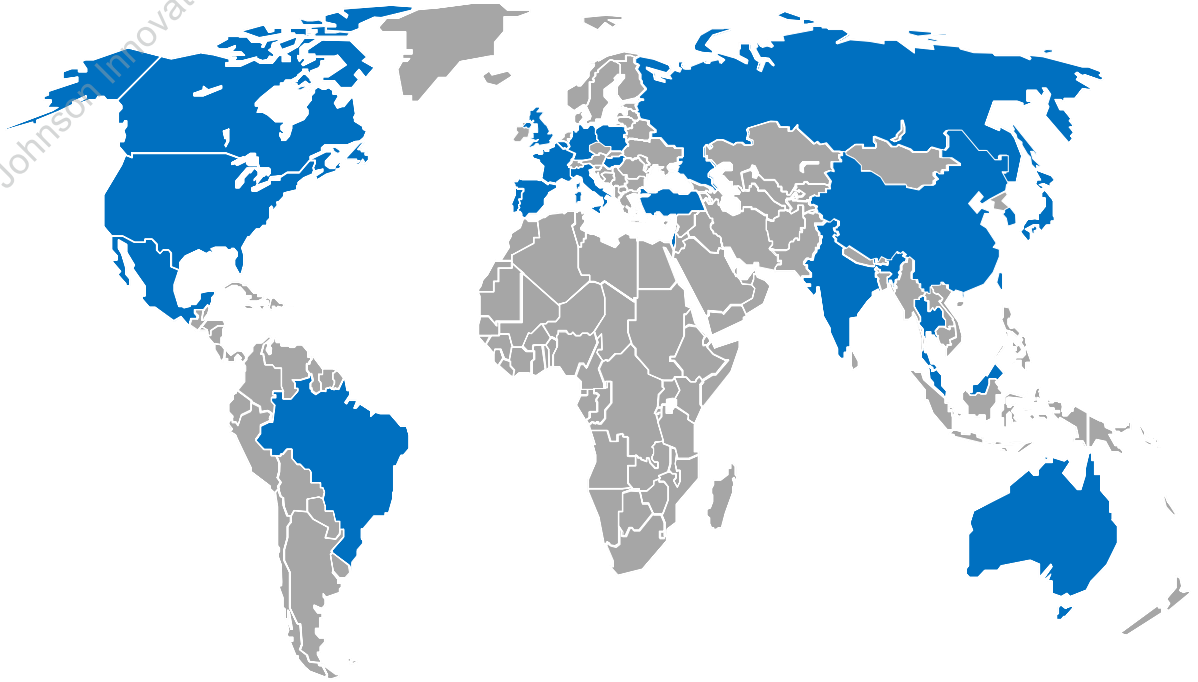
1L, first-line; Ex20ins, exon 20 insertion; IPCW, inverse probability of censoring weighting.

1. Zhou C, et al. *N Engl J Med.* 2023;389(22):2039–2051.

Acknowledgments

- Participants who were enrolled in the study and their families and caregivers
- Physicians and nurses who cared for participants and 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 funded by Johnson & Johnson

A total of 308 participants from 24 countries were randomized in the PAPILLON study



Other Amivantamab Presentations at WCLC 2026

PALOMA-2

First-line Subcutaneous Amivantamab Plus Lazertinib in *EGFR*-mutated Advanced NSCLC: Updated Results From the PALOMA-2 Study

Monday, September 14; 2:25PM–2:33PM
(PT2.03.06; M Nagasaka)

COPERNICUS

Subcutaneous Amivantamab + Lazertinib With Supportive Care in *EGFR*m NSCLC: Longer Follow-Up From the Pragmatic COPERNICUS Study

Tuesday, September 15; 12:00PM–12:05PM
(MO12.09; B Halmos)

2026

Thank You.