8614

COPERNICUS

COPERNICUS, a pragmatic phase 2b study of subcutaneous amivantamab plus chemotherapy with enhanced dermatologic adverse event prophylaxis in *EGFR*-mutated advanced NSCLC: Interim results

Ticiana Leal[1,*], Balazs Halmos[2], Narjust Florez[3], Wade Iams[4], Melissa Johnson[5], Sarah B Goldberg[6], Xiuning Le[7], Sonam Puri[8], Danny Nguyen[9], Luis Raez[10], Jonathan Riess[11], Joshua Sabari[12], David Bjork[13], Nichelle Stigger[14], Ronald Tang[15], Yichuan Xia[16], Paul Cifuentes[17], Farah Shanoon[17], Illse Leipoldt[18], Kartik Konduri[19]

[1]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [2]Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, USA; [3]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; [4]Greco-Hainsworth Centers for Research, Tennessee Oncology, Nashville, TN, USA; [5]Sarah Cannon Research Institute, Nashville, TN, USA; [6]Yale School of Medicine, New Haven, CT, USA; [7]MD Anderson Cancer Center, The University of Texas, Houston, TX, USA; [8]Moffitt Cancer Center, Tampa, FL, USA; [9]City of Hope Orange County Lennar Foundation Cancer Center, Irvine, CA, USA; [10]Memorial Cancer Institute, Pembroke Pines, FL, USA; [11]UC Davis Comprehensive Cancer Center, Sacramento, CA, USA; [12]NYU Langone Health, New York, NY, USA; [13]The Research Evangelist Podcast, Georgetown, MA, USA; [14]LUNGevity Foundation, Chicago, IL, USA; [15]LA Cancer Network, Pasadena, CA, USA; [16]Johnson & Johnson, Wayne, PA, USA; [17]Johnson & Johnson, Horsham, PA, USA; [18]Johnson & Johnson, Durban North, South Africa; [19]SCRI at Texas Oncology, Dallas, TX, USA

*Presenting author: ticiana.a.leal@emory.edu

Key Takeaway

Early success was achieved at the planned interim analysis, demonstrating promising efficacy and improved safety for subcutaneous (SC) amivantamab every 3 weeks (Q3W) + chemotherapy in participants with epidermal growth factor receptor (*EGFR*)–mutated advanced non-small cell lung cancer (NSCLC) after disease progression on an EGFR tyrosine kinase inhibitor (TKI)

Conclusions

The primary endpoint was met, with a median investigator-assessed (INV) progression-free survival (PFS) of 10.4 months

Enhanced dermatologic adverse event (AE) prophylaxis led to substantial reductions in dermatologic AEs and amivantamab interruptions, albeit with a different follow-up duration than in MARIPOSA-2[1]

There were no administration-related reactions (ARRs) observed with SC amivantamab

Please scan QR code

- Poster
- Narrated poster video
- Supplementary material

https://www.congresshub.com/Oncology/AM2026/Amivantamab/Leal

Acknowledgments

We thank the individuals who participated in this study and their families and caregivers, the physicians and nurses who cared for the participants, the staff members who supported this clinical trial, and the staff members at the study sites and those who were involved in data collection/analyses. This study was funded by Janssen Research & Development, a Johnson & Johnson company. Medical writing assistance was provided by Katie Bretland, PhD, of Lumanity Communications Inc., and funded by Johnson & Johnson.

Disclosure

TL served in a consulting or advisory role for AbbVie, Amgen, AstraZeneca, Black Diamond Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Catalyst Pharmaceuticals, Genentech, Gilead, Jazz Pharmaceuticals, Johnson & Johnson, Novartis, Novocure, OncoC4, Pfizer, Regeneron, Sanofi, Synthekine, Roche, and Takeda; received travel, accommodations, and/or expenses from Novocure, Regeneron, and Sanofi; and received research funding from Daiichi Sankyo/AstraZeneca.

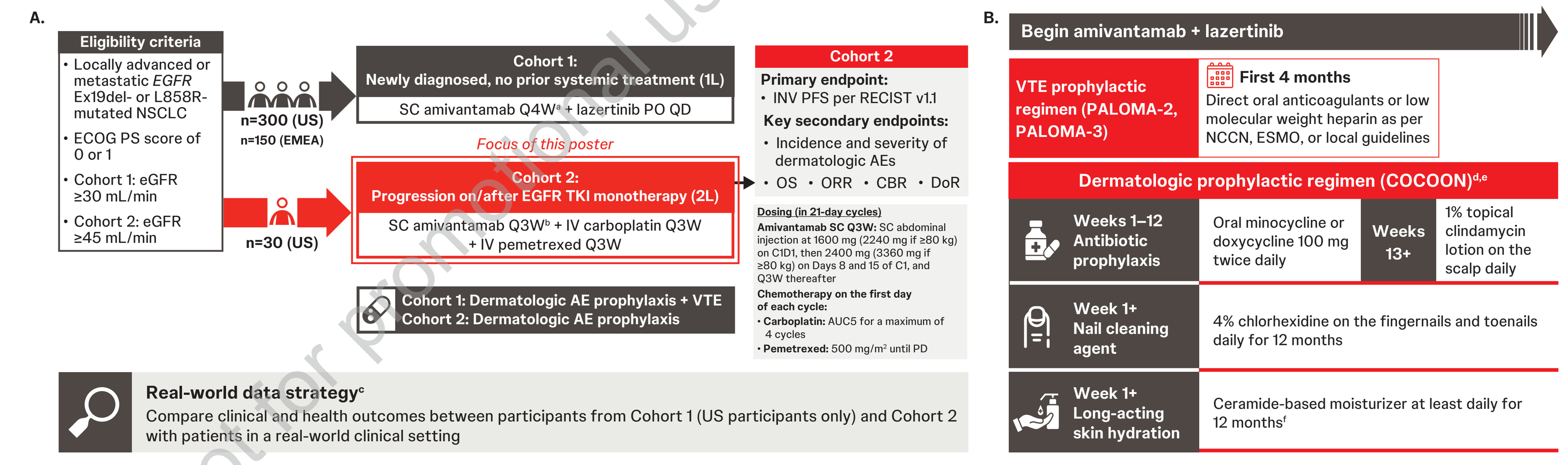
Background

- In MARIPOSA-2 (NCT04988295), 60% of participants with common *EGFR*-mutated advanced NSCLC interrupted intravenous (IV) amivantamab due to AEs, including infusion-related reactions (IRRs) and dermatologic AEs[1,2]
- Despite these interruptions, IV amivantamab in combination with carboplatin-pemetrexed chemotherapy significantly prolonged PFS vs chemotherapy[1]
  - Median blinded independent central review–assessed PFS was 6.3 vs 4.2 months (hazard ratio [HR], 0.48; *P*<0.001)
  - Median INV PFS was 8.2 vs 4.2 months (HR, 0.41)
- Several studies have evaluated different approaches to improve treatment administration and the patient experience with amivantamab
  - In PALOMA-3 (NCT05388669) and PALOMA-2 (NCT05498428), SC amivantamab (co-formulated with recombinant human hyaluronidase PH20) reduced ARRs and treatment administration time (≤5 minutes vs 2–5 hours)[3,4]
    - Based on PALOMA, PALOMA-2, and PALOMA-3 data, SC amivantamab has been approved in several markets, including the US, Europe, Japan, and China[5–8]
  - In COCOON (NCT06120140), an enhanced prophylactic dermatologic regimen significantly reduced grade ≥2 dermatologic AEs vs standard of care (42% vs 75%; *P*<0.0001)[9]
- In COPERNICUS (NCT06667076), we present a protocol-specified interim analysis of SC amivantamab administered Q3W + chemotherapy on or after disease progression on an EGFR TKI in participants with common *EGFR*-mutated advanced NSCLC receiving enhanced dermatologic AE prophylaxis

Methods

- COPERNICUS is one of the largest studies enrolling in the US to evaluate common *EGFR*-mutated advanced NSCLC (**Figure 1A**)
- The pragmatic study design included partnering with academic/community sites, reducing the stringency of inclusion criteria, and streamlining radiology requirements to mirror local practices in the US
- Participants received enhanced dermatologic prophylaxis aligned with the regimen described in COCOON (**Figure 1B**)
  - No prophylactic anticoagulation was required for Cohort 2
- The primary endpoint was INV PFS per Response Evaluation Criteria in Solid Tumors v1.1, estimated using the Kaplan-Meier method
  - The null hypothesis was that the median INV PFS would be ≤4.5 months
- Safety and overall survival (OS) were key secondary endpoints
  - Safety included the incidence and severity of ARRs and dermatologic AEs
- To further characterize these findings, a descriptive comparison of safety findings with data from MARIPOSA-2 was included
- Safety and efficacy in the COPERNICUS study will continue to be evaluated as data mature

Figure 1: (A) COPERNICUS study design and (B) prophylaxis for dermatologic AEs[9]



COPERNICUS (ClinicalTrials.gov Identifier: NCT06667076).
[a]In 28-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. [b]In 21-day cycles until disease progression, withdrawal of consent, or the investigator decides to discontinue treatment, whichever comes first. [c]The real-world comparison will be assessed under a separate protocol. [d]Prophylactic antibiotics: oral doxycycline or minocycline 100 mg BID and topical clindamycin lotion 1% on the scalp daily before bedtime. Paronychia prophylaxis: chlorhexidine 4% on the fingernails and toenails daily. Skin moisturization of the body and face at least daily. [e]Tacrolimus was added as a reactive management recommendation in COPERNICUS based on positive results from the COCOON treatment substudy.[10] In addition, a protocol amendment for COPERNICUS recommended zinc supplementation for participants with established zinc deficiency who experienced dermatologic AEs. [f]La Roche-Posay Lipikar AP+M moisturizer was used in COCOON.

Results

Baseline demographic and clinical characteristics

- As of the clinical cutoff (March 16, 2026), Cohort 2 had completed enrollment with 29 participants in the US
  - Median (range) follow-up was 10.1 (0.5–12.7) months, and 69% of participants were still ongoing in the study
- The pragmatic design supported broad enrollment (**Table 1**)
  - Median age was 62 years, with 45% of participants ≥65 years of age and 21% ≥75 years of age
  - 38% were Asian, 7% were Black or African American, and 21% were Hispanic or Latino

Table 1: Baseline demographic and clinical characteristics

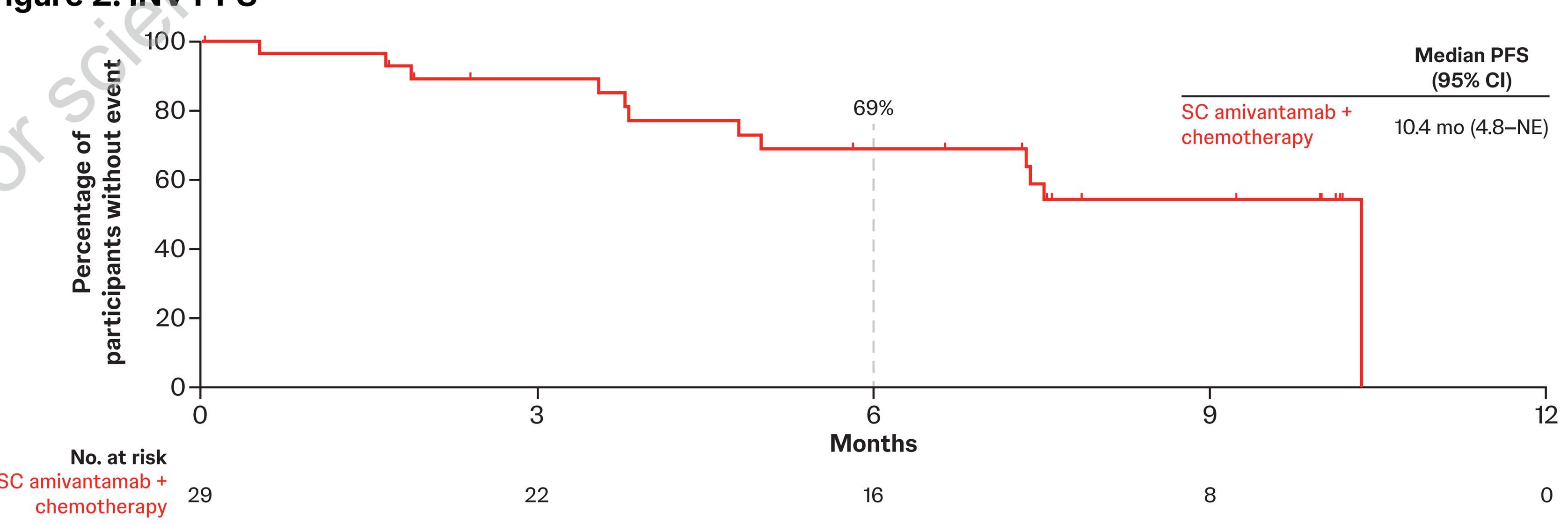
Characteristic, n (%)	SC amivantamab Q3W + chemotherapy (n=29)
Median (range) age, years	62 (39–92)
Age ≥65 years	13 (45)
Age ≥75 years	6 (21)
Female	12 (41)
Race	
White	12 (41)
Asian	11 (38)
Black or African American	2 (7)
Other[a]	4 (14)
Hispanic or Latino	6 (21)
ECOG PS score	
0	11 (38)
1	18 (62)
History of smoking	10 (34)
Brain metastases	8 (28)
***EGFR* mutation type[b]**	
Ex19del	18 (62)
L858R	11 (38)

[a]Other includes unknown (7%) and not reported (7%). [b]Participants may have both Ex19del and L858R.
ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex19del, exon 19 deletion; L858R, exon 21 L858R substitution; Q3W, every 3 week; SC, subcutaneous.

Efficacy

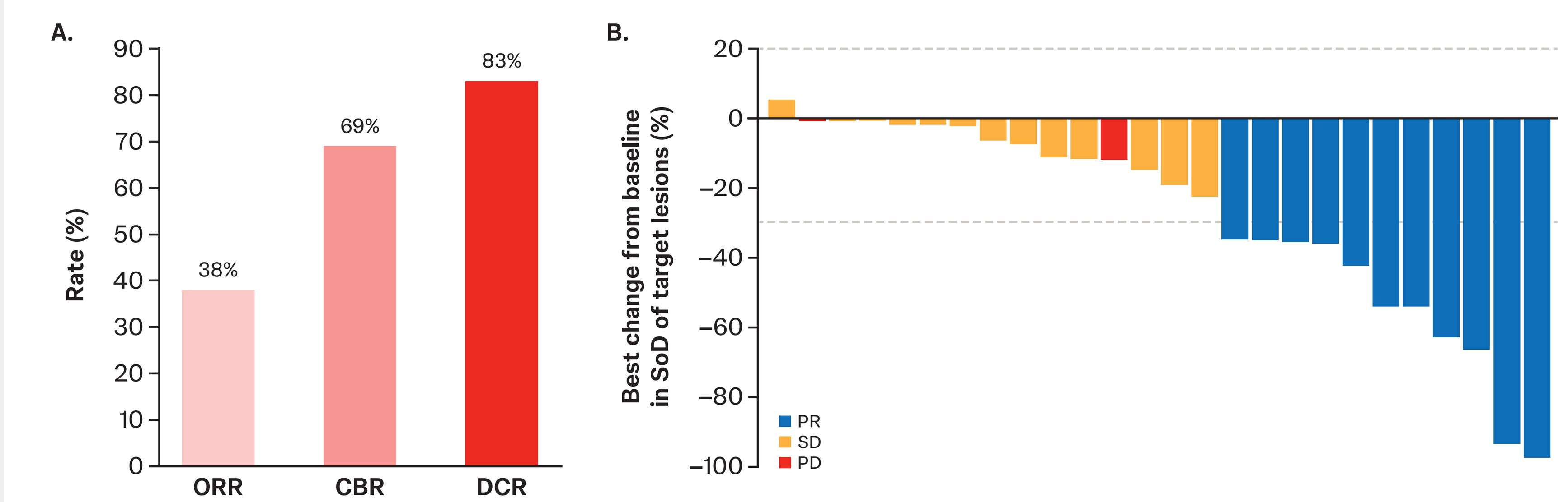
- The primary endpoint was met; median INV PFS was 10.4 months (95% confidence interval [CI], 4.8–not estimable [NE]; **Figure 2**)
- Median OS was immature at this time (NE [95% CI, 11.2–NE])
- Among all participants, INV overall response rate was 38% (95% CI, 21–58; **Figure 3**)
- Clinical benefit rate was 69% (95% CI, 49–85) and disease control rate was 83% (95% CI, 64–94)
- Among responders, median duration of response was 5.6 months (95% CI, 2.8–NE), and in 18% of responses, duration was ≥6 months

Figure 2: INV PFS



CI, confidence interval; INV, investigator-assesesed; NE, not estimable; PFS, progression-free survival; SC, subcutaneous.

Figure 3: (A) Key secondary efficacy endpoints[a] and (B) best percentage (%) change in SoD of target lesions[b]



[a]ORR is defined as % of participants who achieved either a CR or PR using RECIST v1.1 as assessed by investigator. CBR is defined as % of participants who achieved CR, PR, or durable SD of ≥11 weeks duration using RECIST v1.1 as assessed by investigator. DCR is defined as % of participants who achieved CR, PR or SD (regardless of durability of stabilization) using RECIST v1.1 as assessed by investigator.
[b]3 response-evaluable participants with no evaluable target lesion measurements at any postbaseline disease evaluation assessments are not included in the plot.
CBR, clinical benefit rate; CR, complete response; DCR, disease control rate; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SoD, sum of diameters.

Safety

- AEs were mostly grade 1 to 2, with no new safety signals identified (**Table 2**)
- 38% of participants interrupted amivantamab due to AEs; of those, 6 (21% of the total cohort) interrupted due to treatment-related AEs
- With enhanced dermatologic prophylaxis, rash (preferred term) incidence was 21% (none grade ≥3), showing numerical reductions vs MARIPOSA-2 (43% [grade ≥3, 6%])[1]
- No participants experienced ARR, showing a substantial reduction vs IRR observed in MARIPOSA-2 (58% [grade ≥3, 5%])[1]
- 2 participants experienced venous thromboembolism (VTE; 1 grade 2; 1 grade 3); 13 participants had VTE in MARIPOSA-2 (3 grade ≥3)[1]
- Grade ≥3 neutropenia was observed in 17% of participants, which is in line with what has previously been observed with carboplatin-pemetrexed use[11]; 2 participants interrupted amivantamab due to neutropenia

Table 2: TEAEs

TEAEs by preferred term (≥30%), n (%)	SC amivantamab Q3W + chemotherapy (n=29)	
	All grades	Grade ≥3
EGFR-related		
Fatigue	22 (76)	1 (3)
Dermatitis acneiform	11 (38)	2 (7)
Paronychia	9 (31)	0
MET-related		
Peripheral edema	9 (31)	0
Hypoalbuminemia	9 (31)	0
Chemotherapy-related		
Neutropenia	12 (41)	5 (17)
Leukopenia	11 (38)	5 (17)
Anemia	9 (31)	2 (7)
Thrombocytopenia	9 (31)	2 (7)
Other		
Nausea	16 (55)	1 (3)
Constipation	14 (48)	0
Decreased appetite	11 (38)	0
Hypokalemia	10 (34)	0

EGFR, epidermal growth factor receptor; Q3W, every 3 weeks; SC, subcutaneous; TEAE, treatment-emergent adverse event.

References

1. Passaro A, et al. *Ann Oncol.* 2024;35(1):77–90. 2. RYBREVANT® (amivantamab-vmjw) injection, for intravenous use [package insert]. Janssen Biotech, Inc.; 2025. 3. Leighl NB, et al. *J Clin Oncol.* 2024;42(30):3593–3605. 4. Nadal E, et al. Presented at: European Society for Medical Oncology (ESMO) Congress; October 17–21, 2025; Berlin, Germany. 5. RYBREVANT FASPRO™ (amivantamab and hyaluronidase-lpuj) injection, for subcutaneous use [package insert]. Janssen Biotech, Inc.; 2026. 6. RYBREVANT® EPAR [product information]. Janssen-Cilag International NV; 2025. 7. RYBROFAZ® combination subcutaneous injection [package insert]. Janssen Pharmaceutical K.K.; 2025. 8. RYBREVANT FASPRO is for subcutaneous use only [package insert]. Janssen-Cilag AG; 2025. 9. Cho BC, et al. *J Thorac Oncol.* 2025;20(10):1517–1530. 10. Spira AI, et al. Presented at: International Association for the Study of Lung Cancer (IASLC) | American Society of Clinical Oncology (ASCO) North America Conference on Lung Cancer (NACLC); December 5–7, 2025; Chicago, IL, USA. 11. Zhang L, et al. *Thoracic Cancer*. 2014;5(2014):50-56.

Lung Cancer