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Ami-Chemo in
1L *EGFR* Ex20ins+
NSCLC

PAPILLON: *TP53* Co-mutations, Sites of Insertion, and ctDNA Clearance Among Patients With *EGFR* Ex20ins-mutated Advanced NSCLC

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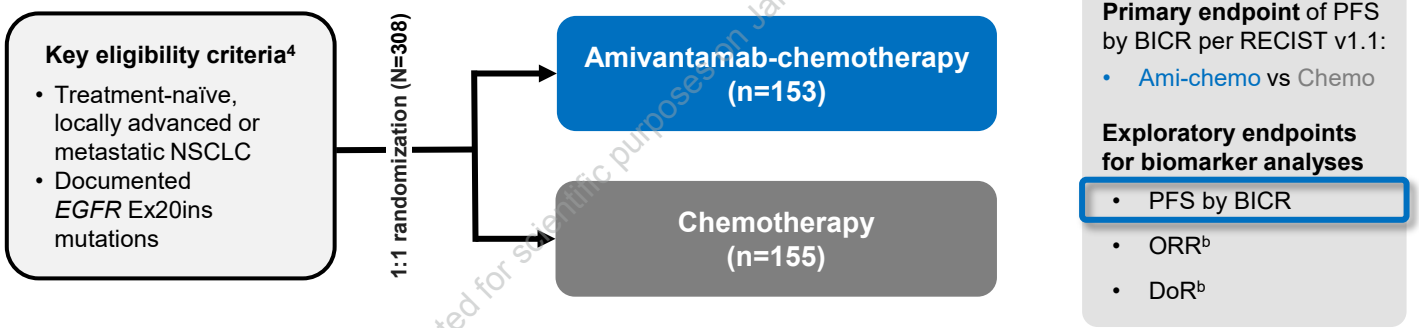
Background and Methods

- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[1–3]
- First-line amivantamab plus chemotherapy significantly improved PFS vs chemotherapy alone in patients with *EGFR* Ex20ins-mutated advanced NSCLC (HR, 0.40 [95% CI, 0.30–0.53]; *P*<0.001) and is approved for use in multiple countries[4–7,a]
- Baseline detectable *EGFR* ctDNA and *TP53* co-mutations are linked to poor prognoses[8–11]
- We evaluated PFS, ORR[b], and DoR[b] among patients from PAPILLON by biomarker subgroups



PAPILLON (ClinicalTrials.gov Identifier: NCT04538664) enrollment period: December 2020 to November 2022; clinical cutoff: May 3, 2023.

[a]Brazil, Canada, Ecuador, Europe, Taiwan, United Kingdom, and the United States. [b]Results not shown.

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. Zhou C, et al. *N Engl J Med*. 2023;389(22):2039–2051. 5. RYBREVANT® (amivantamab-vmjw) injection for intravenous use [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2024. 6. RYBREVANT: EPAR [product information]. Belgium: Janssen-Cilag International NV. 2024. 7. RYBREVANT® Product Monograph, Toronto, ON: Janssen Inc. 2024. 8. Assaf ZJF, et al. *Nat Med*. 2023;29(4):859–868. 9. Provencio M, et al. *Oncotarget*. 2017;9(1):488–494. 10. Song Y, et al. *Transl Lung Cancer Res*. 2020;9(2):269–279. 11. Li XM, et al. *Clin Lung Cancer*. 2021;22(2):100–109.e3.

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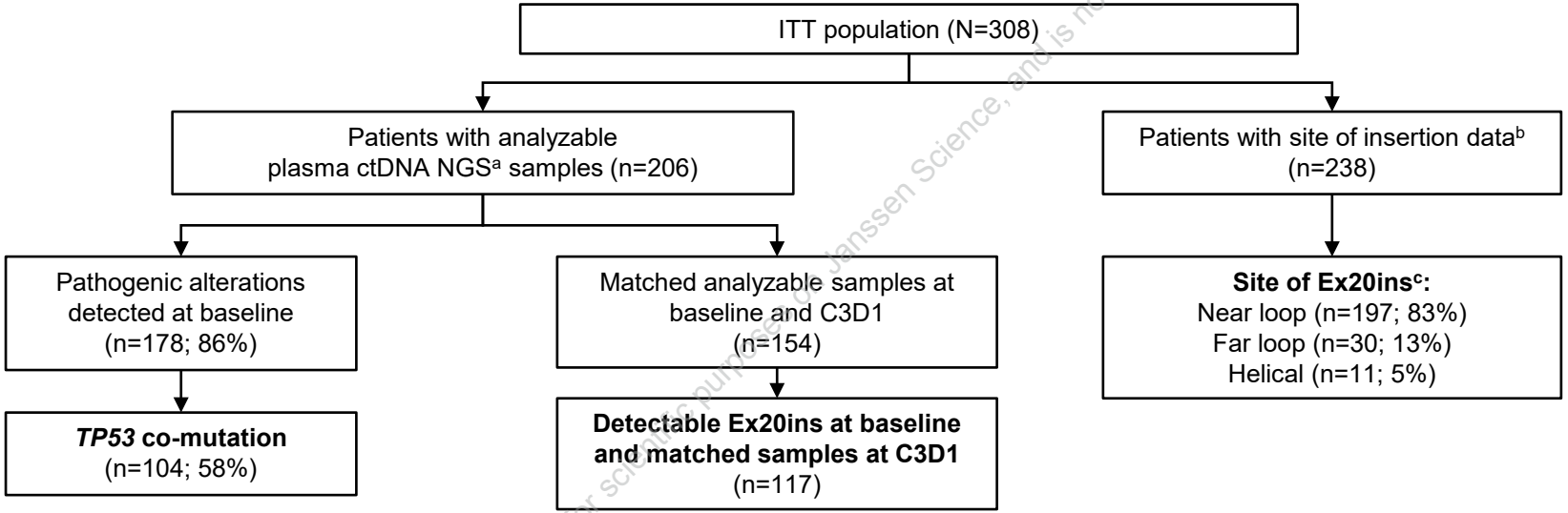
Patient Disposition for Biomarker Analyses



- Ami-chemo reduced the risk of progression or death by >60% over chemo in both the NGS ctDNA analyzable population (HR, 0.35; *P*<0.0001) and the site of insertion population (HR, 0.39; *P*<0.0001), indicating these subgroups were representative of the ITT population

[a]Using Guardant360® CDx, and excluding patients enrolled in China sites who were not analyzable for ctDNA (n=87) and those who did not pass QC (n=15). [b]Using Guardant360® CDx (plasma; global/excluding China sites) or AmoyDx LC10 NGS panel (tissue; China sites).
[c]Ex20ins sites were further grouped into helical (E762–M766), near-loop (A767–P772), and far-loop (H773–C775) regions.

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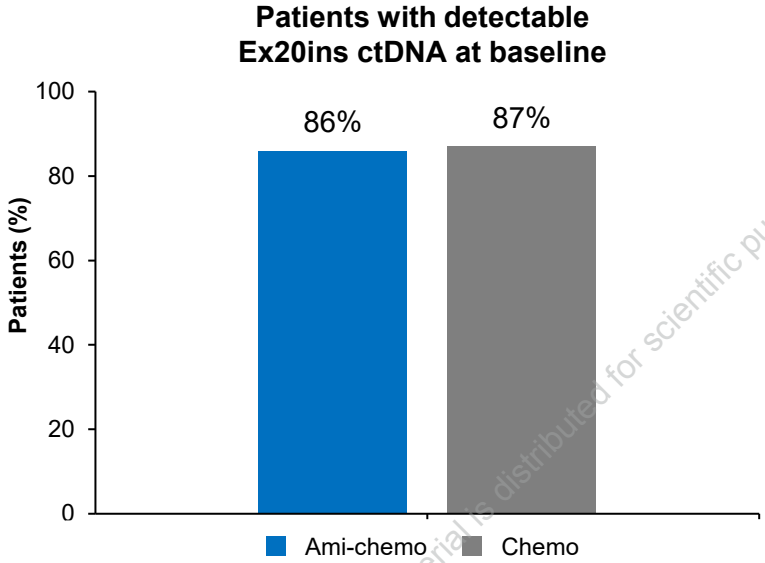
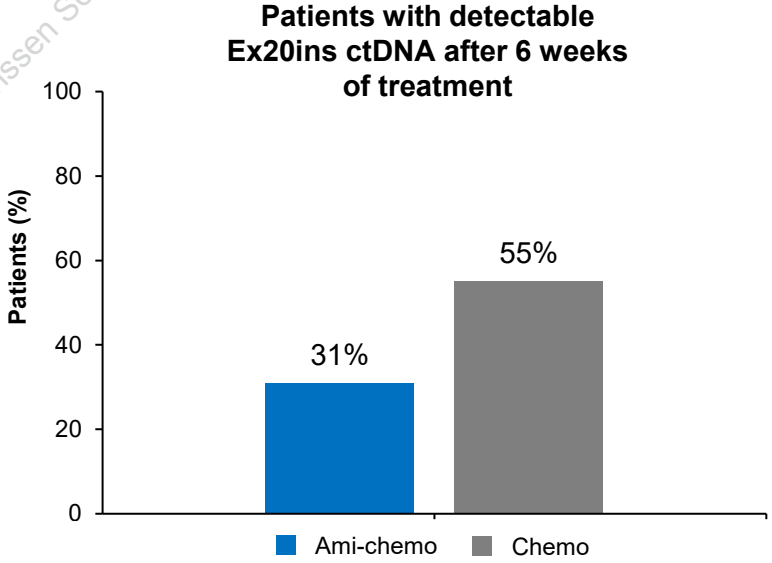
Detectable Ex20ins ctDNA

- The proportion of samples and detection rates at baseline were balanced across both arms
- Among patients with baseline detectable ctDNA:
  - Ami-chemo improved PFS vs chemo (11.1 vs 5.8 mo; HR, 0.38 [95% CI, 0.26–0.55]; *P*<0.0001)
  - More patients exhibited Ex20ins ctDNA clearance in the ami-chemo vs chemo arm after 6 weeks of treatment (C3D1)





C, cycle; ctDNA, circulating tumor DNA; D, day; Ex20ins, Exon 20 insertions.

Detectable Ex20ins ctDNA and ctDNA Clearance (cont'd)

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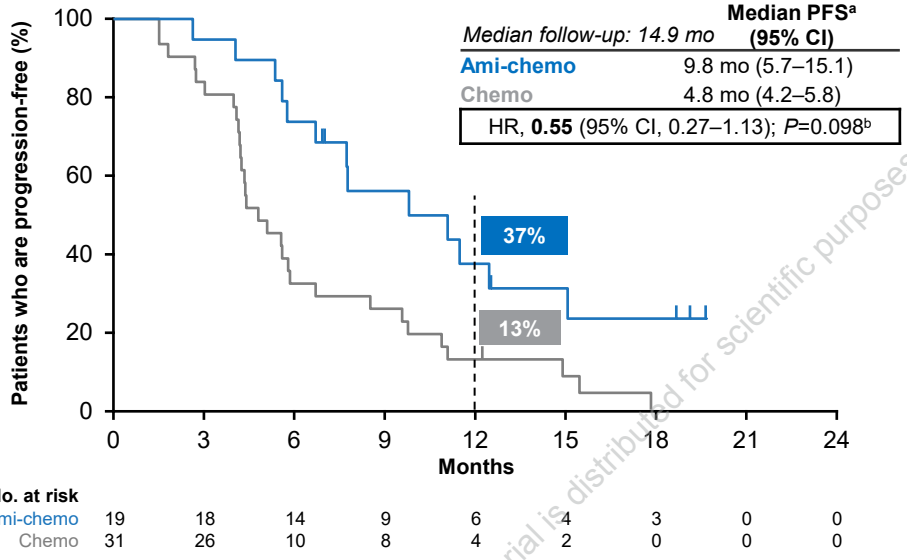
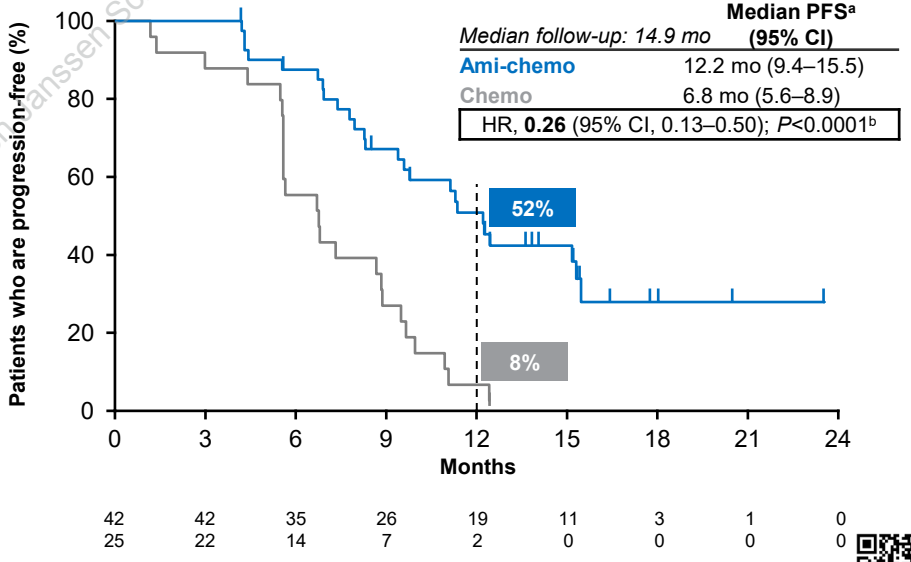
Among patients with baseline detectable ctDNA, PFS favored ami-chemo regardless of ctDNA clearance after 6 weeks of treatment

***Not cleared* Ex20ins ctDNA after 6 weeks of treatment**



***Cleared* Ex20ins ctDNA after 6 weeks of treatment**



[a]Assessed by BICR. [b]Hazard ratio is calculated using a stratified proportional hazards model. *P*-value is calculated using a log-rank test stratified by ECOG PS (0 or 1) and history of brain metastases (yes or no).

TP53 Co-mutations and Wild-type *TP53*

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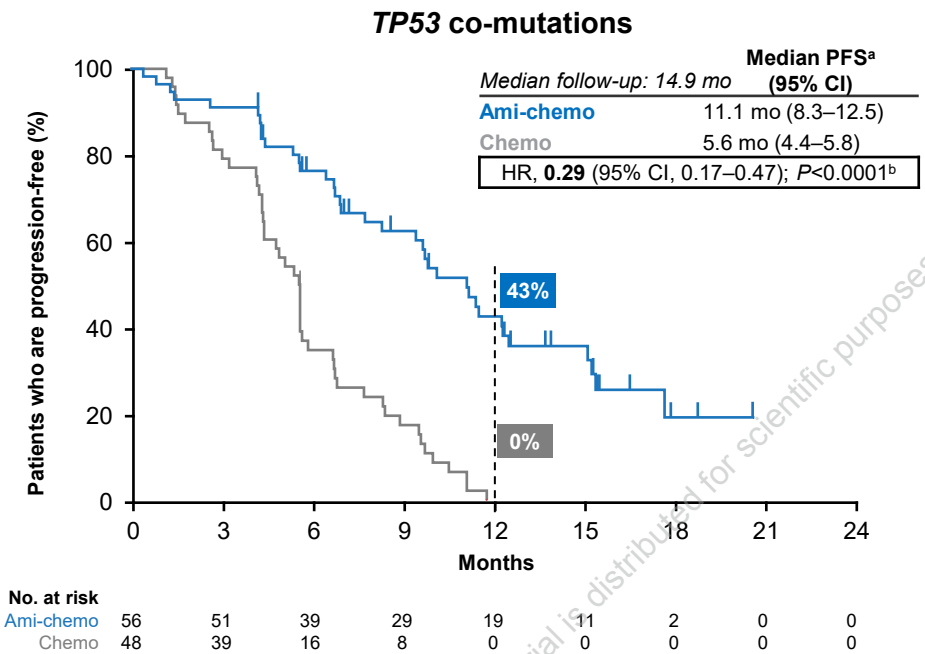
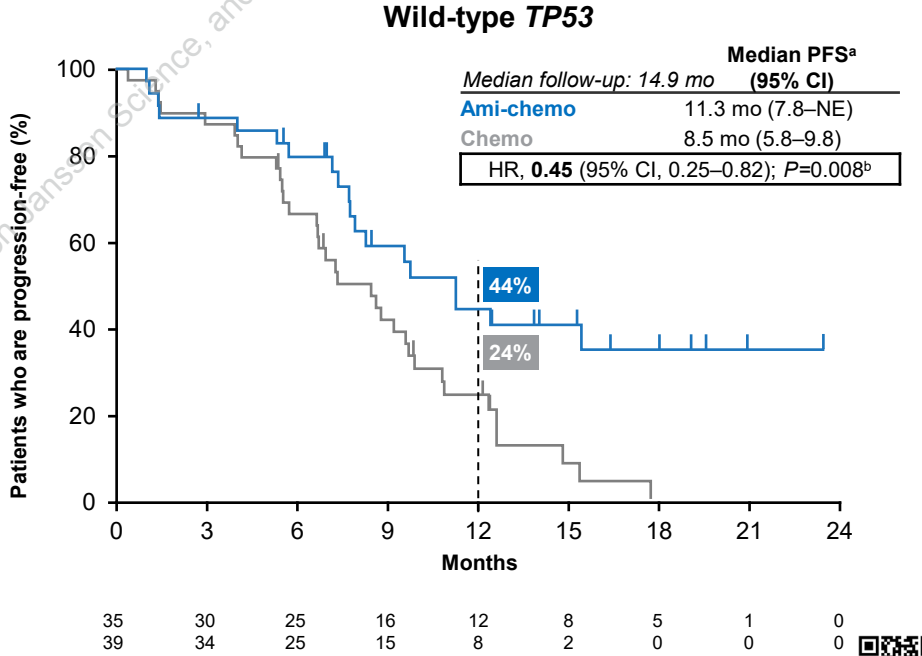
Ami-chemo significantly prolonged PFS in both patients with or without TP53 co-mutations





[a]Assessed by BICR. [b]Hazard ratio is calculated using a stratified proportional hazards model. *P*-value is calculated using a log-rank test stratified by ECOG PS (0 or 1) and history of brain metastases (yes or no).

Exon 20 Sites of Insertion

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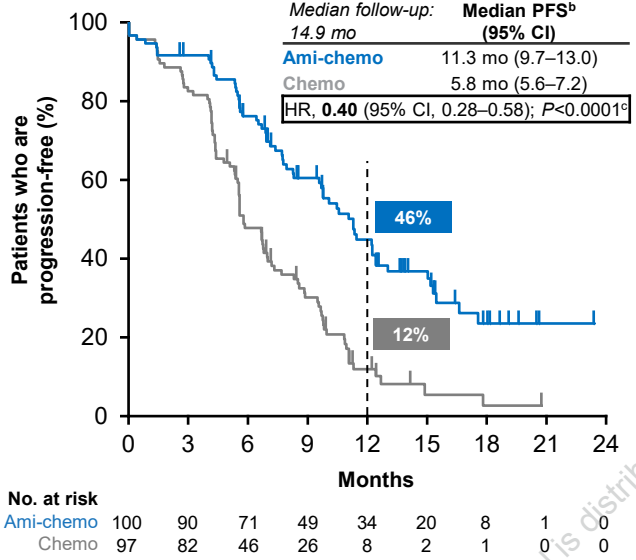
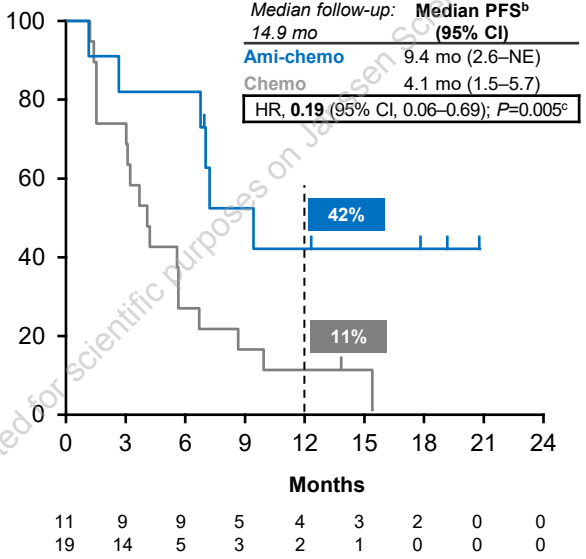
Ami-chemo prolonged PFS vs chemo across the different regions of Ex20ins[a]

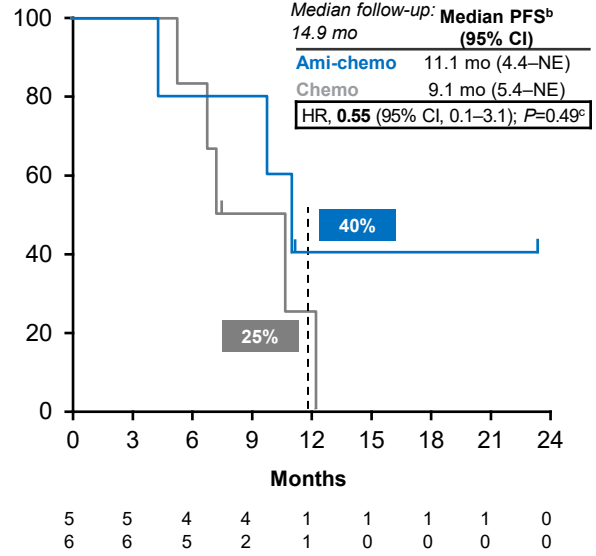
Near loop region (n=197; 83%)



Far loop region (n=30; 13%)



Helical region (n=11; 5%)



[a]Although the sample size was small, a trend towards improved PFS was also observed among those with helical sites of insertion. [b]Assessed by BICR. [c]Hazard ratio is calculated using a stratified proportional hazards model. *P*-value is calculated using a log-rank test stratified by ECOG PS (0 or 1) and history of brain metastases (yes or no).

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Conclusions

- Amivantamab-chemotherapy demonstrated superior treatment outcomes vs chemotherapy across biomarkers of high-risk disease:
  - Detectable ctDNA at baseline (HR, 0.38; *P*<0.0001)
  - Detectable ctDNA after 6 weeks of treatment (HR, 0.55; *P*=0.098)
  - Presence of *TP53* co-mutations (HR, 0.29; *P*<0.001)
- The improvement of PFS with amivantamab-chemotherapy was consistent across subgroups by region of Ex20ins

Amivantamab-chemotherapy is the new first-line standard of care for patients with treatment-naïve, *EGFR* Ex20ins-mutated advanced NSCLC

Other Amivantamab Presentations at WCLC 2024

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MARIPOSA

Longer follow-up of amivantamab + lazertinib vs osimertinib in first-line *EGFR*-mutant advanced NSCLC

Sunday, Sep 8 10:47-10:57am

(OA02.03; Gadgeel)

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)

MARIPOSA

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

Sunday, Sep 8 11:07-11:17am

(OA02.05; Lee)

PALOMA-3

Subcutaneous vs intravenous amivantamab: patient satisfaction and resource utilization results

Monday, Sep 9 11:07-11:17am

(OA09.05; Alexander)

SKIPPirr

Preventing infusion-related reactions with intravenous amivantamab: primary results

Tuesday, Sep 10 2:00-2:05pm

(MA12.08; Lopes)

EGFResisters

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)

Acknowledgments

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- Patients who participated in the study and their families and caregivers
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- Staff members at the study sites and involved in data collection/analyses
- Medical writing assistance was provided by Lumanity Communications Inc. and funded by Janssen Global Services, LLC

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