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A single-arm phase 2 study of first-line amivantamab, lazertinib, pemetrexed in *EGFR*-mutant NSCLC: AMIGO-1 (LACOG 0821)

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Disclosure

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Introduction

- First-line treatment for ***EGFR*-mutant (*EGFR*m) NSCLC** has substantially evolved over the past decade [1-4]
- Intensified therapy has shown improvements in progression-free survival (PFS) and overall survival[2-4]
  - **18-month PFS:**
    - **Osimertinib:** ~50% [1,2,4]
    - **Amivantamab/lazertinib (MARIPOSA):** ~60% [2]
- AMIGO-1 was designed before the MARIPOSA and FLAURA-2 studies were completed and tested the effects of an even more intensified approach in the first-line setting

Study Hypothesis

We hypothesized that adding pemetrexed to amivantamab/lazertinib as first-line treatment in patients with recurrent/metastatic NSCLC with *EGFR* exon 19 or 21 mutations would improve the 18-month PFS rate compared to historical controls.

1. **Ramalingam et al**. N Engl J Med. 2020. doi:10.1056/NEJMoa1913662; 2. **Cho et al.** N Engl J Med. 2024. **doi:**10.1056/NEJMoa2403614; 3. **Yang et al.** *N Engl J Med*. 2025. doi:10.1056/NEJMoa2503001; 4. **Jänne et al.** *N Engl J Med*. 2026;394:27–38. doi:10.1056/NEJMoa2510308.

Study Design

STUDY LACOG 0821 AMIGO-1

Multicenter (13 centers), single-arm, phase 2 trial

ELIGIBILITY CRITERIA

- ✓ Treatment-naïve recurrent/metastatic NSCLC;
- ✓ PS 0-1;
- ✓ *EGFR* exon 19 deletion or exon 21 L858R mutation
- ✓ Asymptomatic or previously treated and stable brain metastases were allowed

N = 49

CYCLE 1 (21-day cycle)	CYCLE 2 (21-day cycle)	CYCLE 3+ (21-day cycle)
Amivantamab 1400mg (1750mg if ≥ 80kg) IV once weekly	**Amivantamab** 1400mg (1750mg if ≥ 80kg) IV on day 1	**Amivantamab** 1750mg (2100mg if ≥ 80kg) IV on day 1
+	+	+
Lazertinib 240mg po daily	**Lazertinib** 240mg PO daily	**Lazertinib** 240mg po daily
+	+	+
Pemetrexed 500mg/m^2 IV on day 1	**Pemetrexed** 500mg/m^2 IV on day 1	**Pemetrexed*** 500mg/m^2 IV on day 1

*In March 2025, the protocol was amended to limit **pemetrexed to 8 cycles**.

Blood samples were collected at **baseline, weeks 6, 12, and 78**, and at **progression** for **ctDNA analysis.**

Primary endpoint:
18-month PFS.

- Patients received dexamethasone prophylaxis (4 mg orally) on the day before, the day of, and the day after each pemetrexed dose (or per local practice).
- Prophylactic anticoagulation was recommended for the first 4 months; anticoagulation beyond 4 months was considered based on individual patient characteristics.
- Prophylactic antibiotic therapy for rash was optional.

Statistical Considerations

- **Primary endpoint**:

  18-month PFS.

- **Secondary endpoint:**

  Overall Survival, ORR.

- **Exploratory analysis:**

  Correlations between baseline tissue- and blood-based biomarkers with outcomes.

- **Sample Size:**

  A one-group chi-square test with a type I error of 0.1 (one-sided) had 80% power to detect the difference between the null hypothesis (18m-PFS of 50%, achieved with osimertinib alone[1]) and the alternative hypothesis (18m-PFS of 65%) with a sample size of 49.

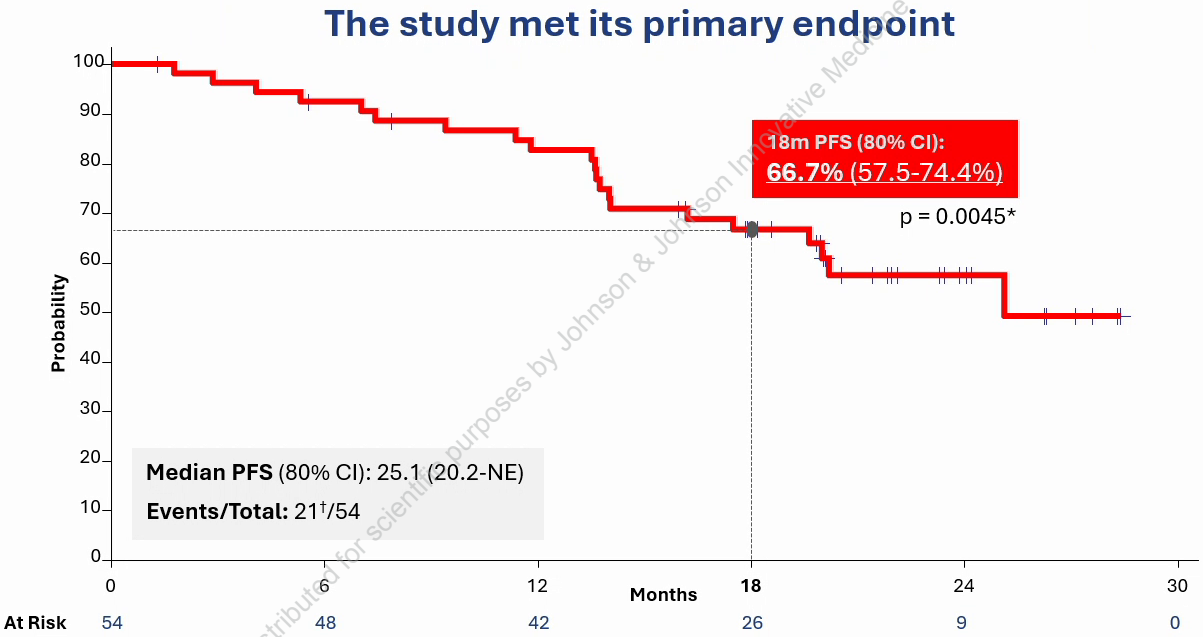
1. **Ramalingam et al**. N Engl J Med. 2020. doi:10.1056/NEJMoa1913662

06 min 20s

Demographic and Baseline Disease Characteristics

Characteristics, n (%)	**All Patients** (N = 54)
Age, in years — Median (range)	**62 (29-79)**
Sex	
Female	35 (65%)
Male	19 (35%)
Race or ethnic group	
White	38 (70%)
Black/Mixed	15 (28%)
Asian	1 (2%)
ECOG performance Status	
0	17 (32%)
1	37 (68%)
History of smoking	
Current/Former	20 (37%)
Never	34 (63%)
Brain metastasis	
No	31 (57%)
Yes	23 (43%)
***EGFR* mutation type**	
Exon 19 deletion	33 (61%)
Exon 21 L858R	21 (39%)

Primary Endpoint: 18m Progression-free Survival



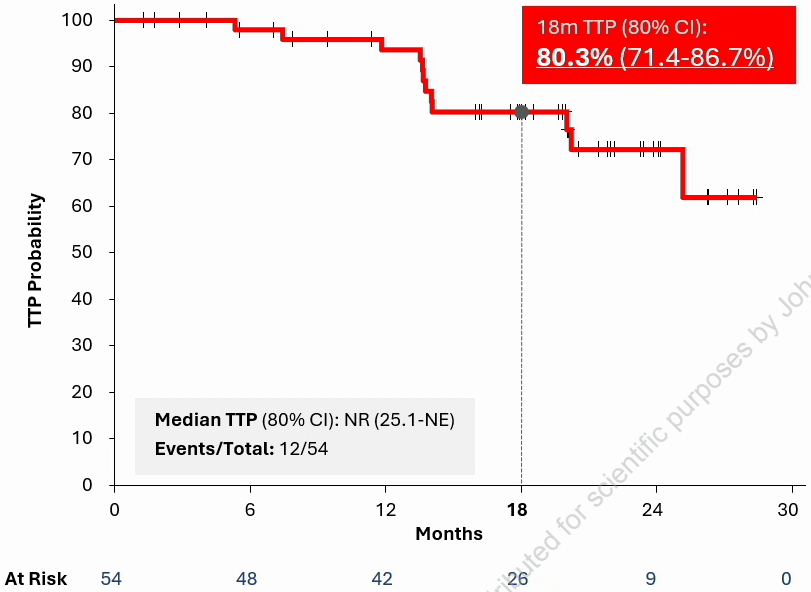
* compared to historical controls (osimertinib monotherapy - FLAURA[1]).

† 9 were deaths before progression (6 treatment-related).

Median follow-up: median follow-up of 22.9 months (IQR: 21.4–23.8). Cutoff date: 1 December 2025 .

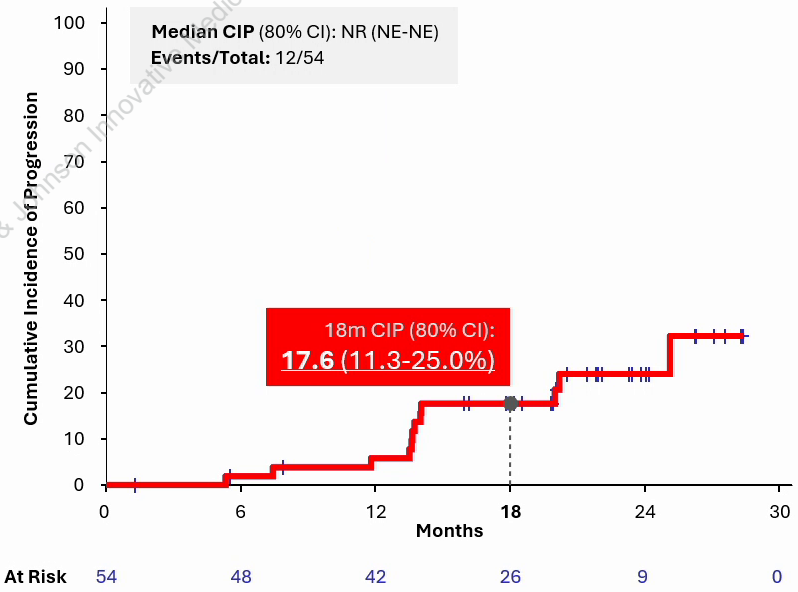
1. **Ramalingam et al.** N Engl J Med. 2020. doi:10.1056/NEJMoa1913662.

Time to Progression



Cumulative Incidence of Progression

with death as competing risk



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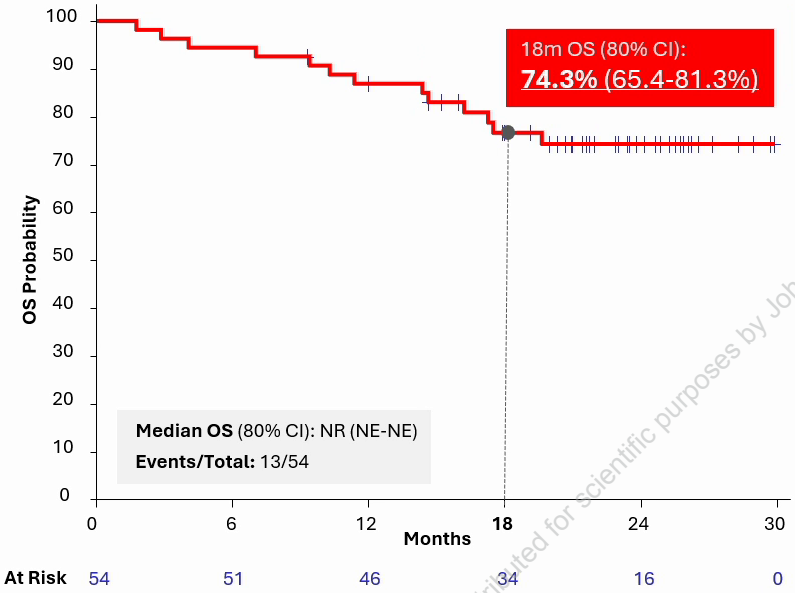
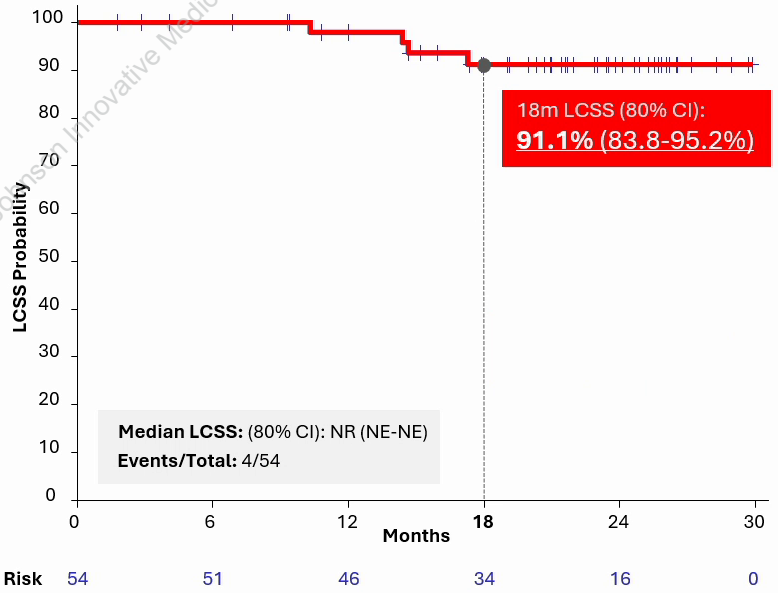
Overall Survival

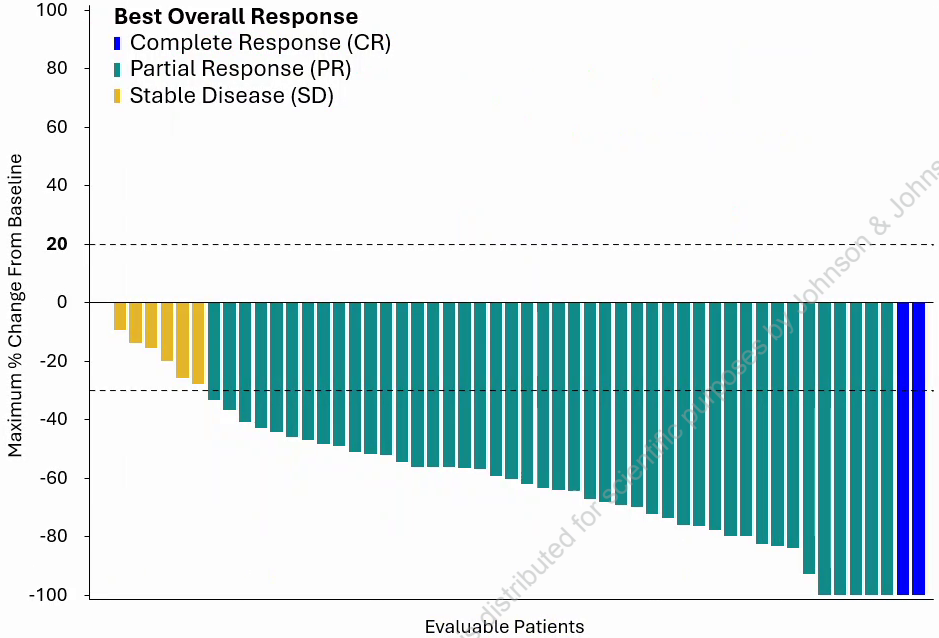


Lung Cancer-specific Survival



Median follow-up: median follow-up of 22.9 months (IQR: 21.4–23.8). Cutoff date: 1 December 2025.

Overall Response Rate



Efficacy Outcome, n (%)	**N = 54***
Overall Response Rate	**46 (85%)**
Best overall response	
Complete Response	2 (4%)
Partial Response	44 (81%)
Stable Disease	7 (13%)
Progressive Disease	0
Not Available*	1 (2%)

*One patient was not evaluable due to study withdrawal prior to the first scheduled assessment.

Median duration of response (months, 95% CI):

NR (23.6 – NR)

NR: not recahed

Median follow-up: median follow-up of 22.9 months (IQR: 21.4–23.8). Cutoff date: 1 December 2025.

Most Common Treatment-related Adverse Events (≥25%)

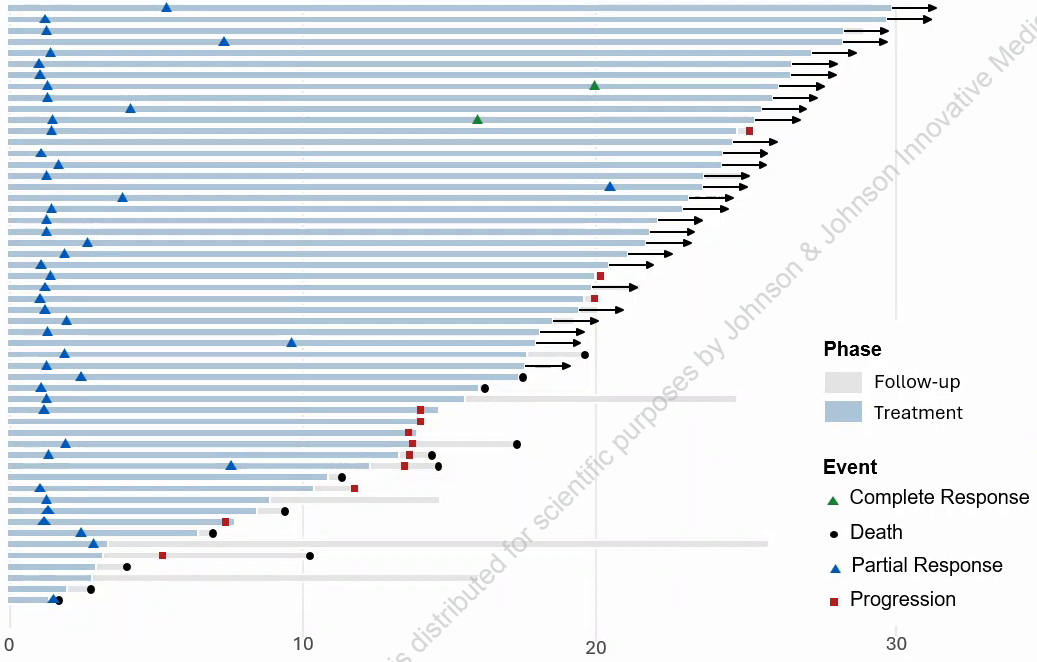
Treatment-related Adverse Events, n (%)	Any Grade	Grade 3	Grade 4
Associated with EGFR inhibition			
Paronychia	44 (81)	8 (15)	0
Rash	35 (65)	14 (26)	0
Stomatitis	29 (54)	5 (9)	0
Diarrhoea	22 (41)	3 (6)	0
Associated with MET inhibition			
Hypoalbuminaemia	43 (80)	9 (17)	0
Peripheral edema	18 (33)	2 (4)	0
Associated with chemotherapy			
Neutropenia‡	34 (63)	17 (31)	11 (20)
Thrombocytopenia	24 (44)	4 (7)	4 (7)
Anemia	29 (54)	10 (19)	1 (2)
Other			
Infusion related reaction	27 (50)	4 (7)	0
Nausea	31 (57)	2 (4)	0
Constipation	16 (30)	0	0
Vomiting	17 (31)	2 (4)	0
Fatigue	21 (39)	5 (9)	0
Asthenia	16 (30)	5 (9)	0
Alanine aminotransferase increased	26 (48)	5 (9)	2 (4)
Aspartate aminotransferase increased	20 (37)	2 (4)	2 (4)
Special Interest AEs			
Rash	35 (65)	14 (26)	0
VTE	8 (15)	1 (2)	0

‡ Febrile neutropenia: 6 (11%)

9 pts experienced Grade 5 AEs:

- 6 (11%) were treatment-related (5 infections, 1 pancreatitis).
- 3 (6%) were not treatment-related (2 infections, 1 aortic stenosis).
- **After safety review, pemetrexed cycles were capped at 8; no further treatment-related deaths occurred.**

Duration of Treatment



Median duration of treatment:
19.9 months (IQR: 13.8–24.1)

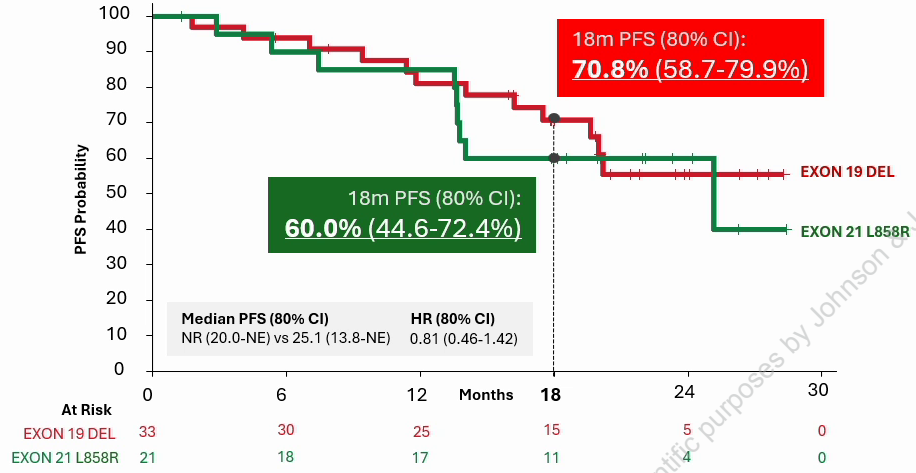
Pemetrexed:
11.5 months (IQR: 6.5–14.1)

Lazertinib:
19.9 months (IQR: 13.8–24.1)

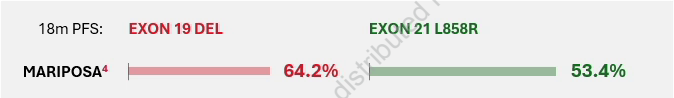
Amivantamab:
12.9 months (IQR: 7.6–17.3)

Median follow-up: median follow-up of 22.9 months (IQR: 21.4–23.8). Cutoff date: 1 December 2025.

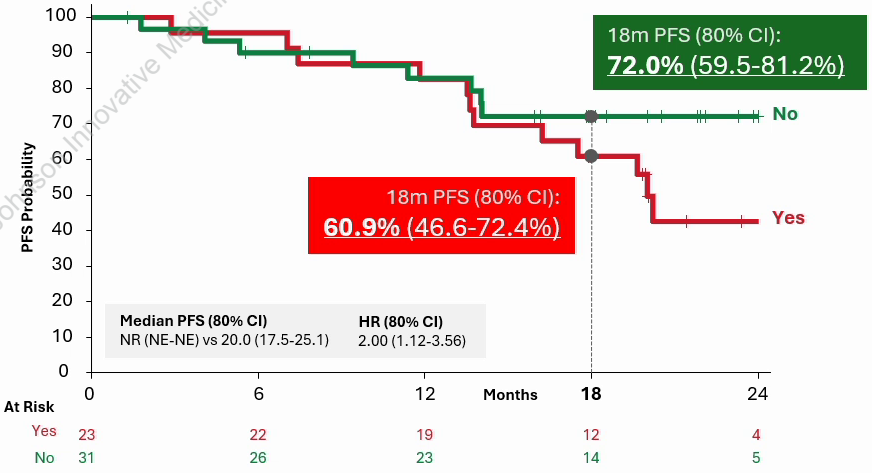
PFS by *EGFR* Mutation



Exploratory contextualization*



PFS by Brain Metastases



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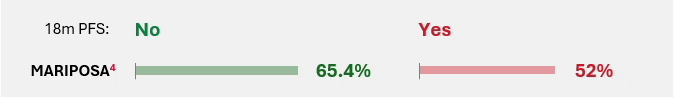


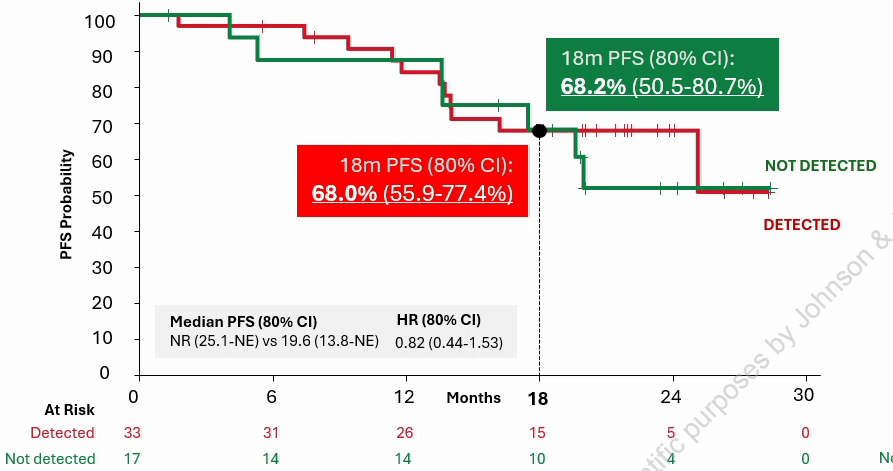
*18-month PFS estimated from the Kaplan–Meier survival curves.

Median follow-up: median follow-up of 22.9 months (IQR: 21.4–23.8). Cutoff date: 1 December 2025.

4. **Enriqueta et al.** J Clin Oncol 42, 2024 (suppl 16; abstr 8504) doi:10.1200/JCO.2024.42.16_suppl.8504

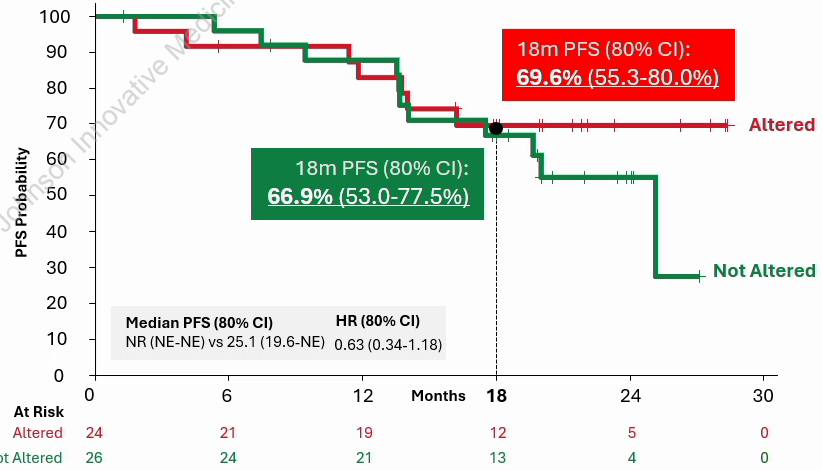
PFS by *EGFR*m ctDNA

(FoundationOne® Liquid)

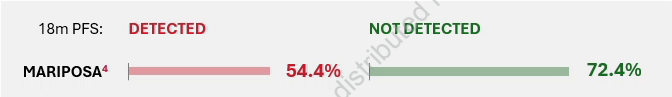


PFS by *TP53* Status

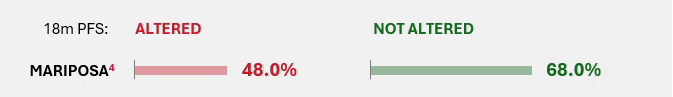
(FoundationOne® Liquid)



Exploratory contextualization*



Exploratory contextualization*



*18-month PFS estimated from the Kaplan–Meier survival curves.

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4. **Enriqueta et al.** J Clin Oncol 42, 2024 (suppl 16; abstr 8504) doi:10.1200/JCO.2024.42.16_suppl.8504

Conclusions

- **AMIGO-1 met its primary endpoint**, demonstrating improved PFS versus historical controls.
- Benefit **appeared more pronounced in poor-prognostic subgroups** (*TP53* co-mutation and detectable baseline EGFRm on liquid biopsy), in which **outcomes seemed numerically higher compared to historical amivantamab plus lazertinib**.
- **Toxicity** may have **limited overall benefit,** but might have been mitigated by pemetrexed adjustments, and could potentially be further diminished by contemporary prophylactic measures.
- If sustained on longer-term follow-up, these findings **may support further evaluation of the modified AMIGO-1 regimen**, especially in patients with poor prognostic features (e.g., *TP53* co-mutations).

Acknowledgments

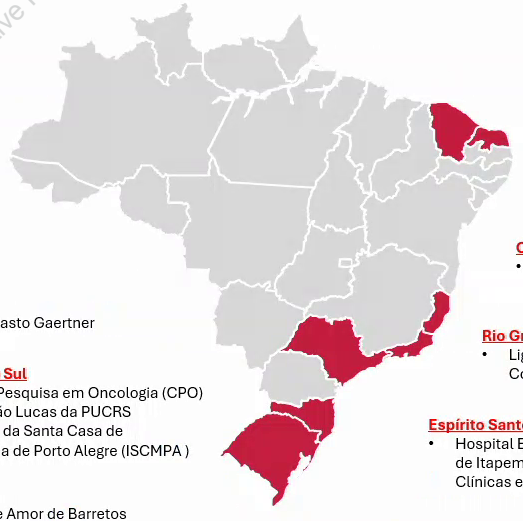
- **Patients** who participated in the study, their families and caregivers.
- **Physicians** and **nurses** who cared for patients and supported this clinical trial.
- **Staff members** at the study sites.
- LACOG Central Office.
- SAS Institute Inc.

Sponsor: LACOG Latin American Cooperative Oncology Group

Co-sponsor: Janssen-Cilag

STUDY LACOG 0821

AMIGO-1 Sites



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- Irmandade da Santa Casa de Misericórdia de Porto Alegre (ISCMPA)

São Paulo
- Hospital de Amor de Barretos
- IBCC Oncologia - Núcleo de Pesquisa São Camilo
- BP - A Beneficência Portuguesa de São Paulo
- FUNFARME - Hospital de Base de São José do Rio Preto
- ICESP - Instituto do Câncer do Estado de São Paulo

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Rio de Janeiro
- CTTB - Centro de Tratamento de Tumores Botafogo (Oncoclínicas)
- INCA - Instituto Nacional de Câncer

Thank You.