Amivantamab Plus Chemotherapy vs Chemotherapy as First-Line Treatment in EGFR Exon 20 Insertion-mutated Advanced NSCLC: Analysis of Post-Progression Endpoints From PAPILLON

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Conclusions

Ami-chemo significantly prolonged TTD and TTST vs chemo. Ami-chemo is the new first-line standard of care for *EGFR* Ex20ins-mutant advanced NSCLC.

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Poster

https://www.congresshub.com/oncology/DGHO2024#product-amivantamab

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Background

- Amivantamab (ami) is an EGFR-MET bispecific antibody with immune cell-directing activity. In PAPILLON (NCT04538664), ami plus carboplatin-pemetrexed (ami-chemo) significantly prolonged progression-free survival (PFS) vs chemo in patients (pts) with EGFR Ex20ins advanced NSCLC (Zhou NEJM 2023). We evaluated post-progression secondary endpoints of time to treatment discontinuation (TTD) and time to subsequent (systemic anticancer) therapy (TTST).

Methods

- 308 pts were randomized (ami-chemo: 153; chemo: 155). Chemo-randomized pts were allowed crossover upon blinded independent central review (BICR)-confirmed progression. TTD and TTST were evaluated based upon site reporting of participant treatment changes.

Results

- At a median follow-up of 14.9 months (mo), 54% (83/153) and 85% (131/155) of pts discontinued treatment in the ami-chemo and chemo arms, respectively. Median TTD was 13.2 mo for ami-chemo vs 7.5 mo for chemo (HR, 0.38 [95% CI, 0.28–0.51]; P<0.0001). Median TTST was 17.7 mo for ami-chemo vs 9.9 mo for chemo (HR, 0.35 [95% CI, 0.25–0.49]; P<0.0001). These findings are consistent with PFS after first subsequent therapy (PFS2; HR, 0.49 [95% CI, 0.32–0.76]; P=0.001) and interim overall survival (HR, 0.67 [95% CI, 0.42–1.09]; P=0.11) favoring ami-chemo vs chemo (Girard Ann Oncol 2023).
- Among pts who discontinued, 52% (43/83) and 72% (94/131) in the ami-chemo and chemo arms started a subsequent therapy, most common being chemotherapy (ami-chemo; 30% [13/43]) and ami monotherapy (chemo; 76% [71/94]). 17% (11/63 with disease progression) of pts continued treatment beyond progression in the ami-chemo arm, median duration after progression of 40.4 weeks (95% CI, 8.7–NE).
- Among 71 chemo-randomized pts who received second-line ami monotherapy, 65 pts were part of the study crossover arm, with 6 receiving ami off protocol. Among the 65 pts in the crossover arm, 46% (30/65) discontinued ami monotherapy. Median treatment duration was 4.9 mo (range, 0–18.2), with a median TTD of 9.7 mo (95% CI, 6.7–11.0).

Phase 3 PAPILLON study (NCT04538664)

Key eligibility criteria
- Treatment-naïve, locally advanced or metastatic NSCLC
- Documented EGFR Ex20ins
- ECOG PS 0 or 1

1:1 Randomization[a] (N=308)

- Amivantamab-Chemotherapy (n=153)
- Chemotherapy (n=155)

Dosing (in 21-day cycles)

Amivantamab: 1400 mg weekly (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)

Chemotherapy on the first day of each cycle:
- Carboplatin: AUC5 for the first 4 cycles
- Pemetrexed: 500 mg/m^2 until disease progression

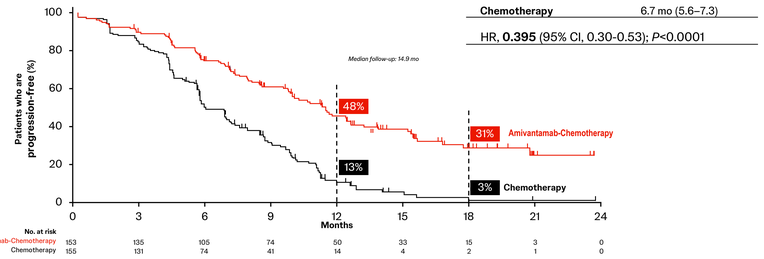
Primary endpoint[b]: Progression-free survival (PFS) by BICR according to RECIST v1.1

Secondary endpoints[b]:
- Objective response rate (ORR)
- Duration of response (DoR)
- Overall survival (OS)
- PFS after first subsequent therapy (PFS2)
- Time to symptomatic progression (TTSP)
- Time to treatment discontinuation (TTD)
- Time to subsequent therapy (TTST)
- Safety

Optional crossover to 2L amivantamab monotherapy[c]

Primary endpoint: Progression-free survival by BICR

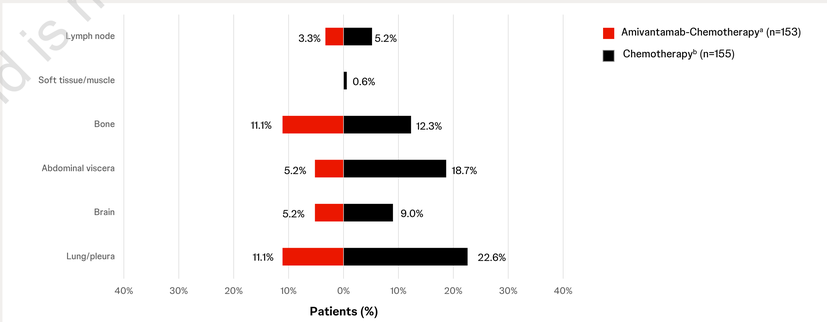
- At a median follow-up of 14.9 months, amivantamab-chemotherapy significantly reduced the risk of progression or death by 60% and improved median PFS by 4.7 months



	Median PFS (95% CI)
Amivantamab-Chemotherapy	11.4 mo (9.8–13.7)
Chemotherapy	6.7 mo (5.6–7.3)
HR, **0.395** (95% CI, 0.30-0.53); *P*<0.0001	

Sites of first progression

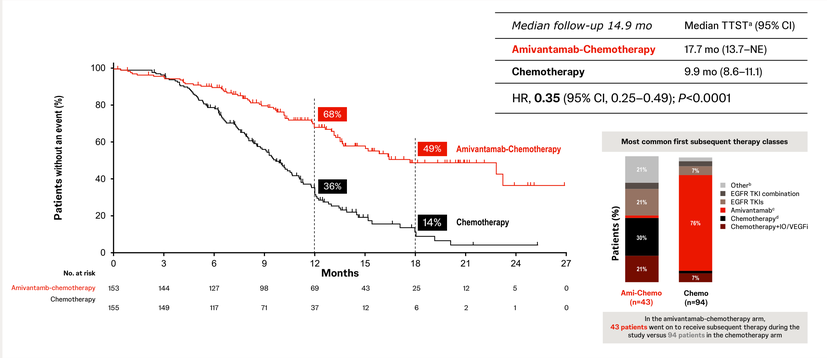
- Rates of progression at all sites were lower with amivantamab-chemotherapy compared to chemotherapy



[a]Among 45 patients who progressed on amivantamab-chemotherapy, there were 55 sites of progression. [b]Among 83 patients who progressed on chemotherapy, there were 106 sites of progression.

Time to subsequent therapy

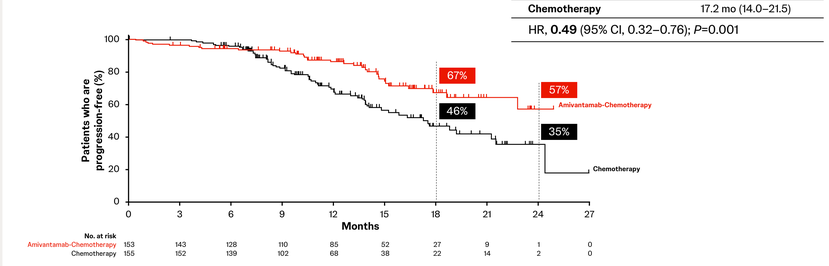
- Median TTST was longer with amivantamab-chemotherapy compared to chemotherapy



Median follow-up 14.9 mo	Median TTST[a] (95% CI)
Amivantamab-Chemotherapy	17.7 mo (13.7–NE)
Chemotherapy	9.9 mo (8.6–11.1)
HR, **0.35** (95% CI, 0.25–0.49); *P*<0.0001	

PFS after first subsequent therapy (PFS2)

- Amivantamab-chemotherapy reduced the risk of second disease progression or death by 51%



Median follow-up 14.9 mo	**Median PFS[a] (95% CI)**
Amivantamab-Chemotherapy	NE (22.8–NE)
Chemotherapy	17.2 mo (14.0–21.5)
HR, **0.49** (95% CI, 0.32–0.76); *P*=0.001	

Originally presented by E Felip at the European Lung Cancer Congress; March 20–23 2024; Prague, Czech Republic