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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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DECLARATION OF INTERESTS

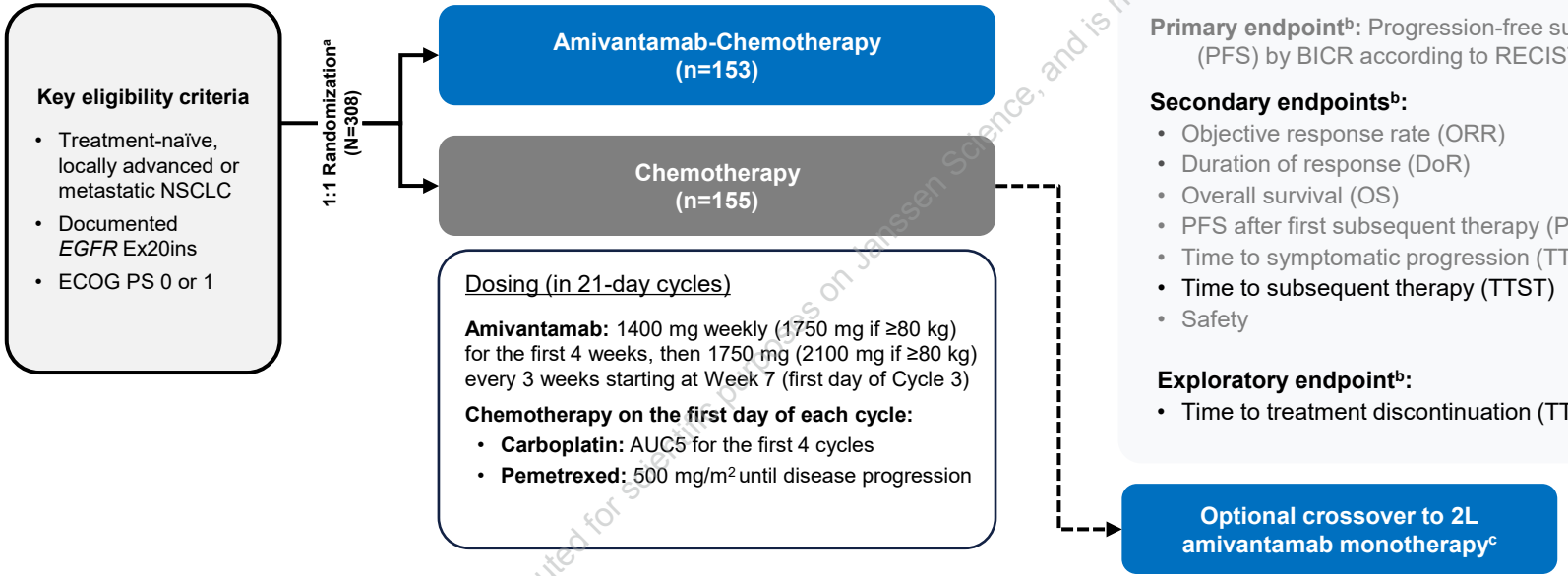
Enriqueta Felip

Advisory role or speaker's bureau: AbbVie, Amgen, AstraZeneca, Bayer, Beigene, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Eli Lilly, F. Hoffman-La Roche, Genentech, Gilead, GlaxoSmithKline, Janssen, Medical Trends, Medscape, Merck Serono, MSD, Novartis, PeerVoice, Peptomyc, Pfizer, Regeneron, Sanofi, Takeda, and Turning Point Therapeutics

Independent board member: Grifols

Phase 3 PAPILLON Study (NCT04538664)

- Amivantamab is an EGFR-MET bispecific antibody with immune cell–directing activity[1-3]



[a]Analyses were further stratified based on ECOG PS, history of brain metastases, and prior EGFR TKI use. Prior EGFR TKI use was later removed as a stratification factor since only 4 patients had prior EGFR TKI use (brief monotherapy with common EGFR TKIs was allowed if lack of response was documented. [b]A hierarchical testing strategy was used for primary and secondary endpoints to control for type 1 error. PFS, ORR, and then OS were included in hierarchical testing. *P* values are nominal for all other secondary and exploratory endpoints. [c]Crossover was only allowed after BICR confirmation of disease progression; amivantamab monotherapy on Q3W dosing per main study.

2L, second line; AUC, area under the curve; BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Ex20ins, Exon 20 insertions; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor.

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.

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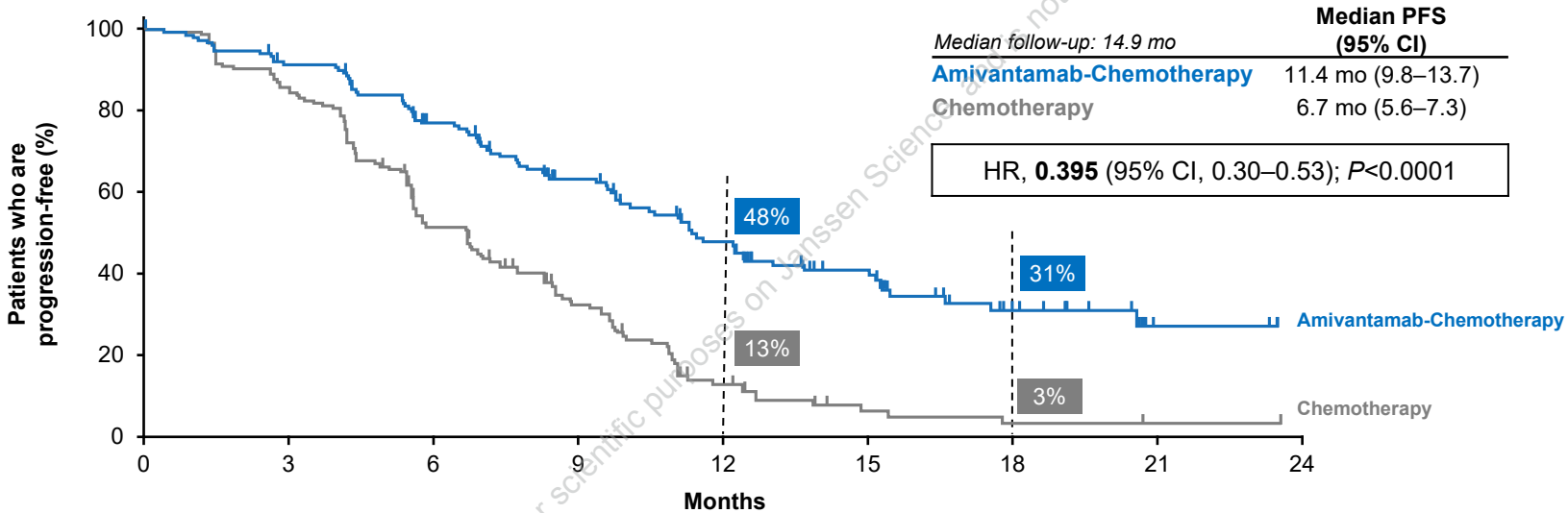
Primary Endpoint: Progression-free Survival by BICR

Amivantamab-chemotherapy is now approved in the US for first-line treatment of EGFR Ex20ins advanced NSCLC[3]



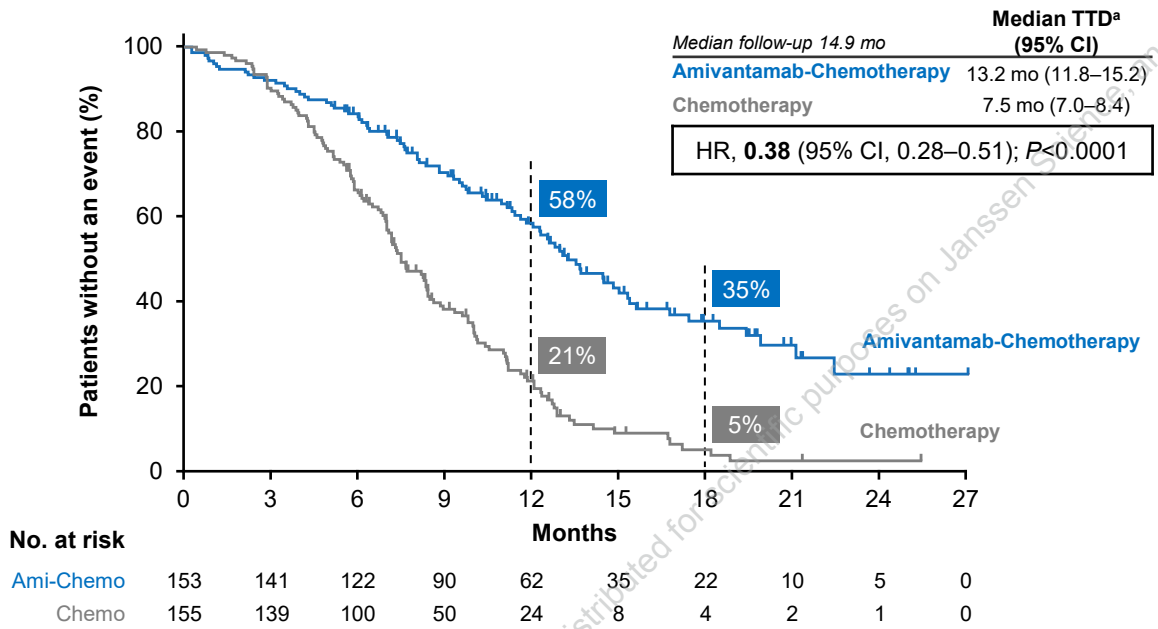
- **Consistent PFS benefit by investigator: 12.9 vs 6.9 mo (HR, 0.38; 95% CI, 0.29–0.51; *P*<0.0001)**

Ami-Chemo, Amivantamab-Chemotherapy; BICR, blinded independent central review; Chemo, Chemotherapy; CI, confidence interval; EGFR, epidermal growth factor receptor; Ex20ins, Exon 20 insertions; HR, hazard ratio; mo, months; NSCLC, non-small cell lung cancer; PFS, progression-free survival; US, United States.

1. Zhou C, et al. *N Engl J Med*. 2023;389(22):2039–2051. 2. Girard N, et al. Presented at:: European Society for Medical Oncology (ESMO) 20-24 October 2023; Madrid, Spain. 3. U.S. Food & Drug Administration. *FDA*. Published online March 1, 2024. Accessed March 7, 2024. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-amivantamab-vmjw-egfr-exon-20-insertion-mutated-non-small-cell-lung-cancer-indications.

Time to Treatment Discontinuation

Median TTD was longer with amivantamab-chemotherapy compared to chemotherapy

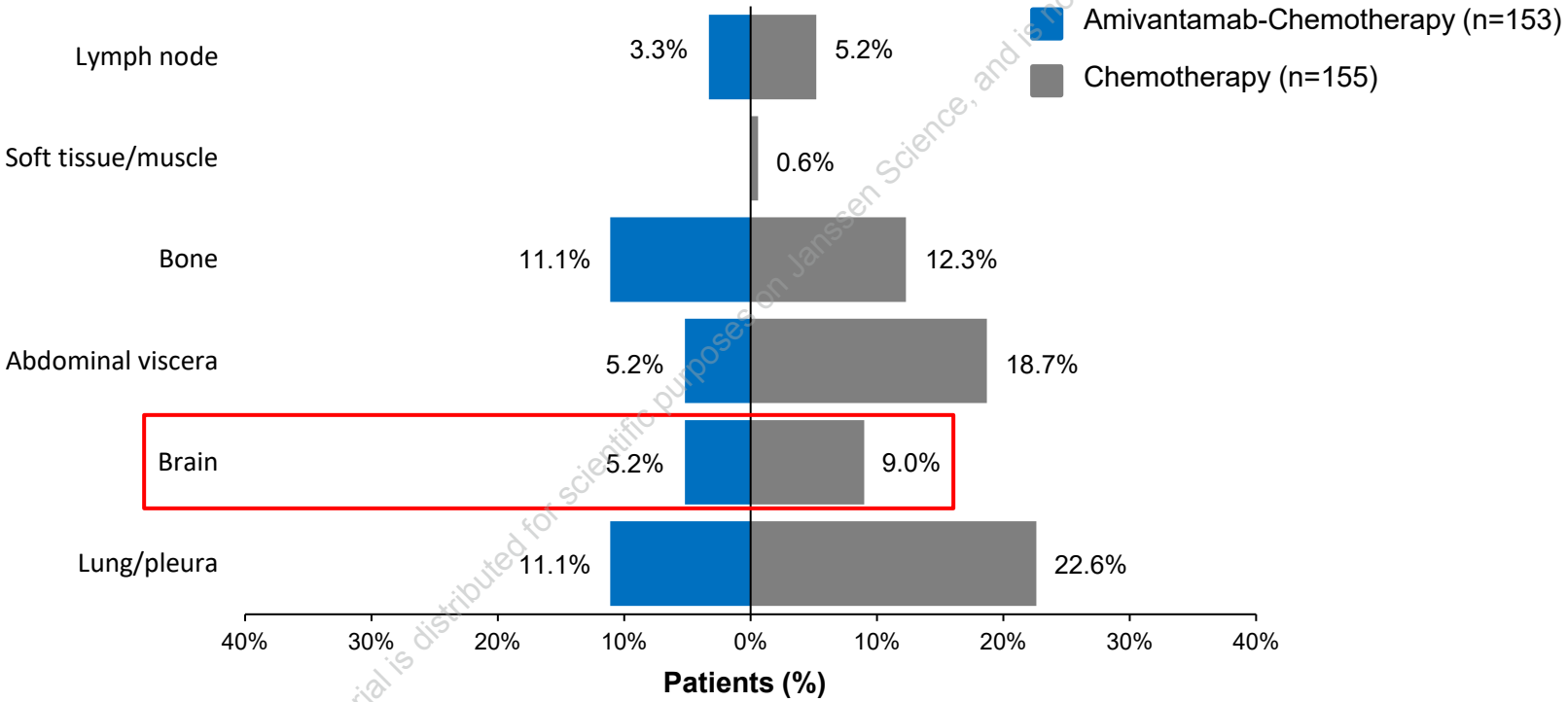


- In the amivantamab-chemotherapy arm, **54% (83/153)** of patients versus **85% (131/155)** in the chemotherapy arm discontinued treatment
  - The primary reason for discontinuation was progressive disease: **33%** of patients in the amivantamab-chemotherapy arm vs **69%** of patients in the chemotherapy arm
- In the amivantamab-chemotherapy arm, **11** patients were treated beyond progression for a median duration of **40.4 weeks (95% CI, 8.7–NE)**[b]

[a]TTD was defined as the time from randomization to discontinuation of all study treatments for any reason. [b]Only included patients that continued study treatment >28 days beyond disease progression.
Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; mo, months; NE, not estimable; TTD, time to treatment discontinuation.

Sites of First Progression

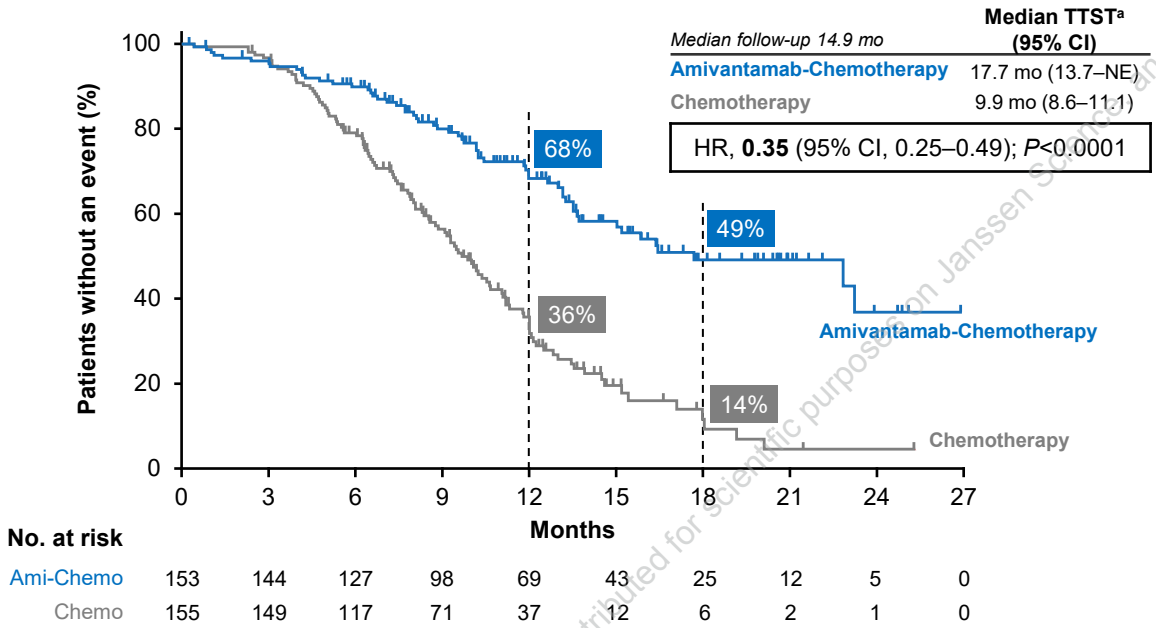
Rates of first progression at all sites were lower with amivantamab-chemotherapy compared to chemotherapy



Note: Each patient can have multiples sites of progression at first disease progression.

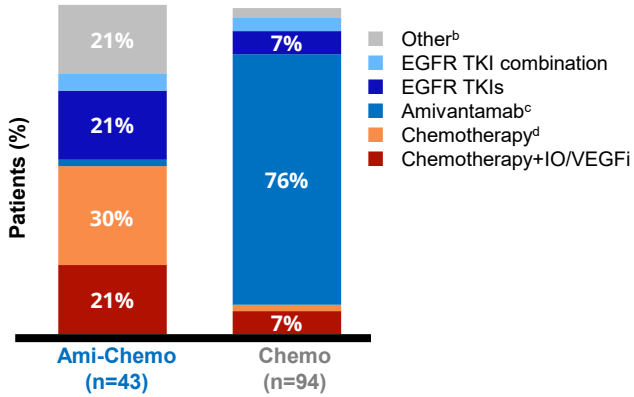
Time to Subsequent Therapy

Median TTST was longer with amivantamab-chemotherapy compared to chemotherapy



Most Common First Subsequent Therapy Classes

- In the amivantamab-chemotherapy arm, **43 patients** went on to receive subsequent therapy during the study versus **94 patients** in the chemotherapy arm



[a]TTST was defined as the time from the date of randomization to the start date of the first subsequent anticancer therapy following study treatment discontinuation or death, whichever occurred first. [b]Other category included IO alone and investigational agents. [c]Six patients received amivantamab monotherapy off-protocol. [d]In the amivantamab-chemotherapy and chemotherapy arms, 23% and 1% of patients received single-agent chemotherapy, respectively, and 7% and 1% of patients received doublet chemotherapy, respectively.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; EGFR, epithelial growth factor receptor; HR, hazard ratio; IO, immuno-oncology; mo, months; NE, not estimable; TKI, tyrosine kinase inhibitor; TTST, time to subsequent therapy; VEGFi, vascular endothelial growth factor inhibitor.

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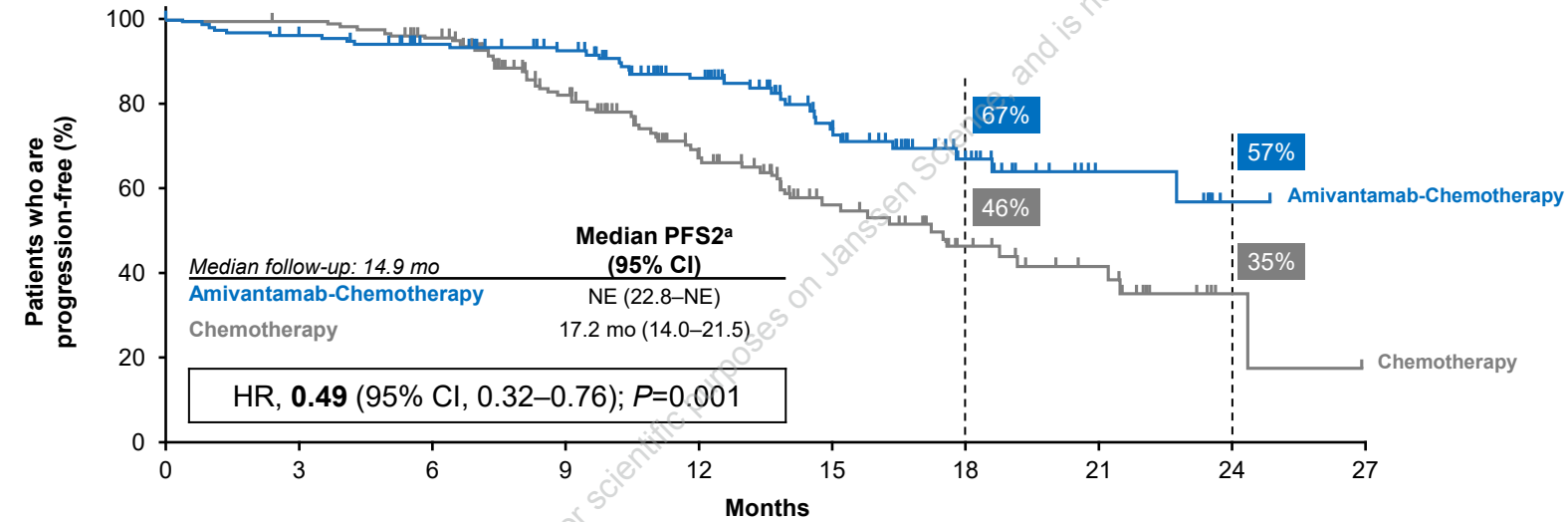
PFS After First Subsequent Therapy (PFS2)

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



[a]PFS2 was defined as the time of randomization until the time of second objective disease progression (based on investigator assessment) or death, whichever occurred first, after the initiation of the first subsequent anticancer systemic therapy.

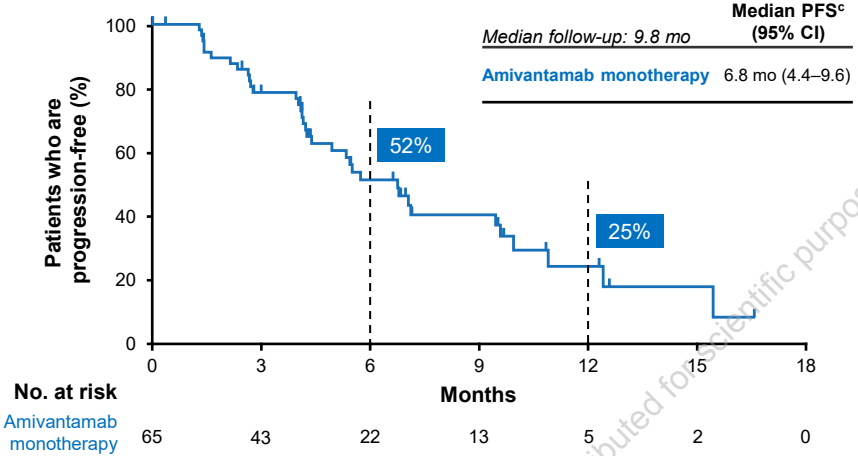
Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; mo, months; NE, not estimable; PFS, progression-free survival.

1. Zhou C, et al. *N Engl J Med*. 2023;389(22):2039–2051. 2. Girard N, et al. Presented at: European Society for Medical Oncology (ESMO) 20-24 October 2023; Madrid, Spain.

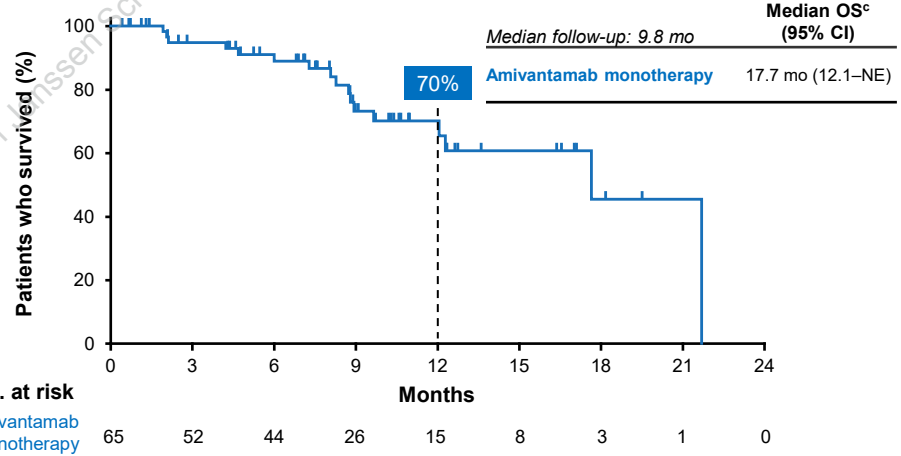
Crossover to 2L Q3W Amivantamab Monotherapy[a]

- Q3W amivantamab monotherapy (n=65) showed a mPFS of 6.8 mo and a mOS of 17.7 mo (median follow-up: 9.8 mo)
- Median TTD[b] was 9.7 mo (95% CI, 6.7–11.0) and median TTST[b] was 9.7 mo (95% CI, 7.7–12.1)
- Safety and efficacy for Q3W amivantamab was consistent with the Q2W results from CHRYSALIS in post-platinum *EGFR* Ex20ins advanced NSCLC[1]

PFS: Progression-free Survival



OS: Overall Survival[d]



[a]66% (71/107) of patients who progressed on first-line chemotherapy received amivantamab monotherapy, including 6 patients who received amivantamab off-protocol. [b]TTD and TTST were defined as the time from first administration of amivantamab monotherapy until the date of treatment discontinuation or start of (second) subsequent therapy, respectively. [c]PFS and OS were defined as the time from first administration of amivantamab monotherapy until the date of objective disease progression or death, whichever occurred first, or death, respectively. [d]There were 17 deaths reported in the crossover arm.

1L, first- line; 2L, second-line; CI, confidence interval; EGFR, epidermal growth factor receptor; Ex20ins, Exon 20 insertions; mo, months; mOS, median overall survival; mPFS, median progression-free survival; NE, not estimable; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks; TTD, time to treatment discontinuation; TTST, time to subsequent therapy.

1. Garrido P, et al. *J Thorac Oncol*. 2023;18(4S):S35–S88.

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Conclusions

- Compared to chemotherapy, **amivantamab-chemotherapy** as first-line treatment of patients with *EGFR* Ex20ins advanced NSCLC significantly prolonged:
  - Time to treatment discontinuation (**13.2 months** vs 7.5 months; HR, 0.38; *P*<0.0001)
  - Time to subsequent therapy (**17.7 months** vs 9.9 months; HR, 0.35; *P*<0.0001)
- The most common subsequent therapies were:
  - Chemotherapy after amivantamab-chemotherapy
  - Q3W amivantamab-monotherapy due to the crossover design after chemotherapy
- In the crossover arm, efficacy results for Q3W amivantamab monotherapy were consistent with the Q2W results from the post-platinum *EGFR* Ex20ins group from the CHRYSALIS study[1]

Amivantamab-chemotherapy is the new first-line standard of care for *EGFR* Ex20ins advanced NSCLC

BICR, blinded independent central review; EGFR, epidermal growth factor receptor; Ex20ins, Exon 20 insertions; HR, hazard ratio; NSCLC, non-small cell lung cancer; PFS, progression-free survival; Q2W, every 2 weeks; Q3W, every 3 weeks.

1. Garrido P, et al. *J Thorac Oncol*. 2023;18(4S):S35–S88.

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