FPN: 7P

Patient-relevant Endpoints From PAPILLON: Amivantamab Plus Chemotherapy vs Chemotherapy as First-line Treatment of *EGFR* Exon 20 Insertion–mutated Advanced NSCLC

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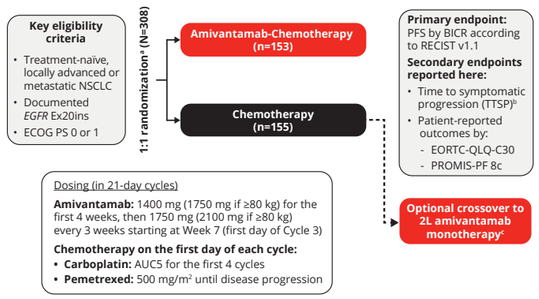
BACKGROUND

- Amivantamab is an epidermal growth factor receptor (EGFR)-MET bispecific antibody with immune cell–directing activity[1–3]
- In PAPILLON (NCT04538664), amivantamab plus carboplatin-pemetrexed (chemotherapy) significantly prolonged progression-free survival vs chemotherapy (hazard ratio [HR], 0.395; *P*<0.0001) in treatment-naïve *EGFR* Exon 20 insertion (Ex20ins) advanced non-small cell lung cancer (NSCLC)[4,5]
- Here, time to symptomatic progression (TTSP) and patient-reported outcomes (PROs) of amivantamab-chemotherapy vs chemotherapy from PAPILLON were evaluated

METHODS

- PAPILLON is a global, randomized, phase 3 trial that compared amivantamab-chemotherapy vs chemotherapy (**Figure 1**)
- Secondary endpoints reported here include TTSP and PROs measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30) and Patient-Reported Outcomes Measurement Information System Short Form Physical Function 8c (PROMIS-PF 8c) instruments
  - TTSP: time from randomization to onset of new/worsening symptoms related to lung cancer (per investigator) and required either a change in treatment and/or clinical intervention, or death

FIGURE 1: Phase 3 PAPILLON study design



[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 a lack of response was documented). [b]Also included death. [c]Crossover was only allowed after BICR confirmation of disease progression; amivantamab monotherapy Q3W dosing per main study.

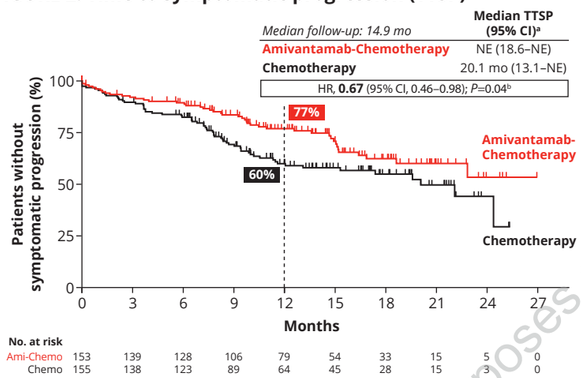
2L, second-line; AUC, area under the curve; BICR, blinded independent central review; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; Ex20ins, Exon 20 insertion; NSCLC, non-small cell lung cancer; PFS, progression-free survival; PROMIS-PF 8c, Patient-Reported Outcomes Measurement Information System Short Form Physical Function 8c; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TKI, tyrosine kinase inhibitor.

Lung Cancer

RESULTS

- Amivantamab-chemotherapy reduced the risk of symptomatic progression by 33% (**Figure 2**)

FIGURE 2: Time to symptomatic progression (TTSP)

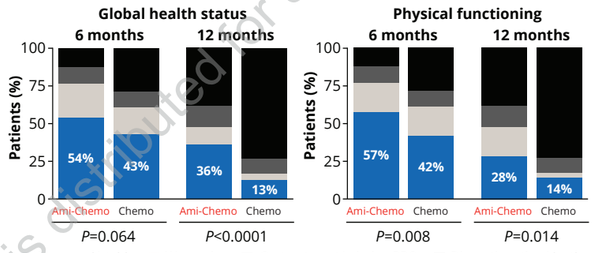


[a]Median TTSP of the ITT population with 95% CIs calculated using the Kaplan-Meier method. [b]HR with 95% CI calculated using a stratified Cox regression model; *P* value calculated using a stratified log-rank test.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not estimable; TTSP, time to symptomatic progression.

- More patients in the amivantamab-chemotherapy arm reported improved or stable global health status and physical functioning vs chemotherapy at 6 and 12 months (**Figure 3**)
  - Results were consistent for role, emotional, cognitive, and social functioning (all *P*<0.05 at 12 months)

FIGURE 3: Patients reporting improved/stable symptoms at 6 and 12 months by EORTC-QLQ-C30



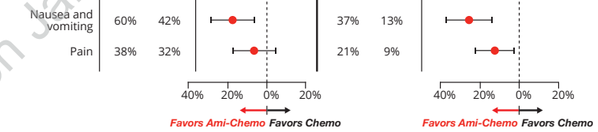
Note: percentages exclude patients with insufficient follow-up. Role functioning is measured by limitation in pursuing work or other daily activities.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; PRO, patient-reported outcome.

- More patients in the amivantamab-chemotherapy arm reported absence of key symptoms vs chemotherapy (**Figure 4**)

FIGURE 4: Patients reporting absence of key symptoms at 6 and 12 months by EORTC-QLQ-C30

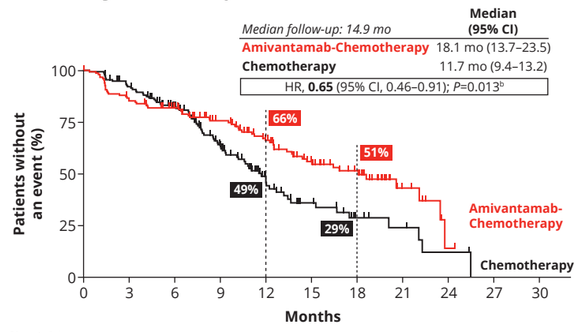
Symptom	6 months Ami-Chemo	6 months Chemo	12 months Ami-Chemo	12 months Chemo
Appetite loss	47%	34%	26%	13%
Constipation	41%	41%	25%	11%
Diarrhea	71%	50%	43%	17%
Dyspnea	45%	26%	22%	6%
Fatigue	19%	9%	6%	4%
Insomnia	48%	31%	25%	9%
Nausea and vomiting	60%	42%	37%	13%
Pain	38%	32%	21%	9%



Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; EORTC-QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire.

- Amivantamab-chemotherapy prolonged time to sustained deterioration in physical functioning vs chemotherapy (**Figure 5**)

FIGURE 5: Time to sustained deterioration[a] in physical functioning over time by PROMIS-PF 8c



[a]Time to sustained deterioration was defined as the time from randomization until the date of the first clinically meaningful deterioration (ie, decrease of ≥6.5 points relative to baseline on the PROMIS-PF 8c total score) or death that is not subsequently followed by a score above the meaningful deterioration threshold at any later visits. [b]Kaplan-Meier analyses of PROs are influenced by disease progressions, which are not part of the definition, and patients post progression have fewer PRO data than those prior to progression. Patients in the chemotherapy arm who entered the crossover phase were censored at the time of the last visit prior to receiving amivantamab.

Ami-Chemo, Amivantamab-Chemotherapy; Chemo, Chemotherapy; CI, confidence interval; HR, hazard ratio; PRO, patient-reported outcome; PROMIS-PF 8c, Patient-Reported Outcomes Measurement Information System Short Form Physical Function 8c.

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KEY TAKEAWAY

Amivantamab-chemotherapy demonstrated improvements in time to symptomatic progression and key patient-reported outcomes compared to chemotherapy among patients with treatment-naïve, *EGFR* Ex20ins–mutated advanced NSCLC

CONCLUSIONS

- Amivantamab-chemotherapy significantly prolonged time to symptomatic progression vs chemotherapy (NE vs 20.1 mo; HR, 0.67; *P*=0.04)
- More patients in the amivantamab-chemotherapy arm reported improved/stable functioning and absence of key symptoms vs chemotherapy based on the EORTC-QLQ-C30
- Amivantamab-chemotherapy prolonged time to sustained deterioration in physical functioning vs chemotherapy (18.1 vs 11.7 mo) based on the PROMIS-PF 8c

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DISCLOSURES

L. Paz-Ares: attended advisory boards for Roche, Merck Sharp & Dohme, Merck Serono, Bristol Myers Squibb, AstraZeneca, Lilly, Pfizer, PharmaMar, Bayer, Amgen, Janssen, GSK, Novartis, Takeda, Sanofi, Mirati Therapeutics, BeiGene, Daiichi Sankyo, Medscape, and PER; had other consulting roles for Genomica and Altum Sequencing; is a member of the board of directors for Stab Therapeutics; and received research funding from Daiichi Sankyo, AstraZeneca, Merck Sharp & Dohme, Bristol Myers Squibb, Janssen-Cilag International NV, Novartis, Roche, Sanofi, Amgen, Tesaro, Alkermes, Lilly, Takeda, Pfizer, PharmaMar, AACR, ASCO, AECC, ASEICA, ESMO, ONCOSUR, and Small Lung Cancer Group. **R. Veillon:** received research funding to the institution from AstraZeneca, AbbVie, Merck Serono, Bristol Myers Squibb, Sanofi, GSK, Novartis, Gilead, Roche, and Janssen; received consulting fees from Merck Sharp & Dohme and Janssen; received payment or honoraria from Roche, AstraZeneca, Bristol Myers Squibb, Merck Sharp & Dohme, Pfizer, Takeda, and Sanofi; and received support for attending meetings and/or travel from Janssen, Takeda, and Sanofi. **M. Majem:** received research funding from Roche, Bristol Myers Squibb, and AstraZeneca; received payment or honoraria from Roche, AstraZeneca, Merck Sharp & Dohme, Amgen, Bristol Myers Squibb, Pierre Fabre, Casen Recordati, Janssen, and Novartis; and received support for attending meetings and/or travel from Merck Sharp & Dohme, Roche, and AstraZeneca. **C. Zhou:** received consulting fees from Innovent Biologics, Qilu, Hengrui, and TopAlliance Biosciences Inc.; and received payment or honoraria from Lilly China, Sanofi, Boehringer Ingelheim, Roche, Merck Sharp & Dohme, Qilu, Hengrui, Innovent Biologics, Alice C-Stone, LUYE Pharma, TopAlliance Biosciences Inc., Amoy Diagnostics, and AnHeart. **K-J. Tang**, **S.-W. Kim**, and **G. Richardson:** have no disclosures to report. **N. Girard:** received consulting fees from AbbVie, Amgen, AstraZeneca, BeiGene, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Gilead, Hoffmann-La Roche, Janssen, Leo Pharma, Lilly, Merck Sharp & Dohme, Novartis, Sivan, Mirati Therapeutics, Pfizer, Sanofi, and Takeda; received payment or honoraria from AbbVie, Amgen, AstraZeneca, BeiGene, Boehringer Ingelheim, Bristol Myers Squibb, Daiichi Sankyo, Gilead, Hoffmann-La Roche, Janssen, Leo Pharma, Lilly, Merck Sharp & Dohme, Novartis, Sivan, Mirati Therapeutics, Pfizer, Sanofi, and Takeda; received support for attending meetings and/or travel from Janssen, Amgen, and Bristol Myers Squibb; and participated on a data safety monitoring board or advisory board for Hoffman-La Roche. **R.E. Sanborn:** attended advisory boards for AstraZeneca, EMD Serono, Daiichi Sankyo, Lilly Oncology, Janssen, MacroGenics, Sanofi, Regeneron, Mirati Therapeutics, GSK, and G1 Therapeutics; is an invited speaker for Illumina; is a steering committee member for GSK and Janssen; received funding to the institution from Merck, AstraZeneca, and Jounce; and has other financial or nonfinancial interests with Bristol Myers Squibb. **A.S. Mansfield:** received grants or contracts to the institution from Novartis and Verily; received consulting fees from Rising Tide and TRIPTYCH Health Partners Expert Think Tank; received payment or honoraria from Janssen, BeiGene, Chugai Pharmaceutical Co Ltd, Ideology Health LLC, Antoni van Leeuwenhoek Kanker Instituut, AXIS Medical Education, Inc., Janssen, Intellisphere LLC, Answers in CME, University of Miami International Mesothelioma Symposium, and Immunocore; received support for attending meetings and/or travel from Shanghai Roche; participated on a data safety monitoring board or advisory board for AbbVie, AstraZeneca, Bristol Myers Squibb, GenentechRoche, and Takeda Oncology; had a leadership or fiduciary role for Mesothelioma Applied Research Foundation and Friends of Patan Hospital; and has other financial or nonfinancial interests with Bristol Myers Squibb. **K. Park:** attended advisory boards for AstraZeneca, Lilly, Ono Pharmaceutical, Bristol Myers Squibb, Merck Sharp & Dohme, Blueprint Medicines, Amgen, Merck KGaA, LOXO Oncology, AbbVie, Daiichi Sankyo, Boehringer Ingelheim, Janssen, Etsai, and Puma Biotechnology; attended a speaker's bureau for Boehringer Ingelheim; and received research grants from AstraZeneca and MSD Oncology. **J. Sermon**, **J. Schuchard**, **A. Bhattacharya**, **P. Lorenzini**, **M. Baig**, **T. Agrawal**, and **R.E. Knoblauch:** are employees of Janssen and may hold stock in Johnson & Johnson. **A. Ono:** received payment or honoraria from AstraZeneca K.K., Chugai Pharmaceutical Co Ltd, and Ono Pharmaceutical; and received research grants to the institution from AstraZeneca K.K., Chugai Pharmaceutical Co Ltd, and Janssen Pharmaceutical K.K. **J.K. Sabari:** attended advisory boards for AstraZeneca, Genentech, Janssen, Pfizer, Regeneron, Sanofi, Takeda, and Mirati Therapeutics.

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