



Amivantamab-Chemotherapy in Non-Small Cell Lung Cancer with *EGFR* Exon 20 Insertions: Impact of Treatment Crossover and Other Endpoints from the Phase III PAPILLON Study

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Abstract

Background In the PAPILLON study, first-line amivantamab-chemotherapy in epidermal growth factor receptor (*EGFR*) exon 20 insertion-mutated non-small cell lung cancer demonstrated significantly prolonged progression-free survival and favorable overall survival over chemotherapy; a consistent benefit was also observed across some secondary endpoints. However, the complete clinical benefit of first-line amivantamab-chemotherapy is not fully understood, nor is the survival advantage in the presence of per-protocol crossover from chemotherapy to amivantamab after progression.

Objective We aimed to assess time to treatment discontinuation (TTD) and time to subsequent therapy (TTST), at the time of primary analysis for progression-free survival, and the effect of the crossover design on overall survival at the time of interim analysis.

Methods In the phase III PAPILLON study, 308 participants were randomized (amivantamab-chemotherapy, $n = 153$; chemotherapy, $n = 155$). Intravenous amivantamab was administered every 3 weeks. Chemotherapy was administered as carboplatin for four cycles and pemetrexed until disease progression. TTD and TTST were evaluated using Kaplan–Meier and Cox proportional hazards models. Crossover-adjusted survival estimates were generated using three established statistical methods.

Results At a median follow-up of 14.9 months, median TTD was 13.2 versus 7.5 months for amivantamab-chemotherapy versus chemotherapy (hazard ratio [HR] 0.38 [95% confidence interval 0.28–0.51]; nominal $p < 0.0001$). Median TTST was 17.7 versus 9.9 months (HR 0.35 [95% confidence interval 0.25–0.49]; nominal $p < 0.0001$). A total of 65/155 participants crossed over from chemotherapy to amivantamab after progression. The crossover-adjusted overall survival continued to demonstrate a favorable survival benefit for amivantamab-chemotherapy versus chemotherapy with HRs of 0.52–0.60, which is more pronounced than the planned interim intention-to-treat overall survival (HR of 0.67; 95% confidence interval 0.42–1.09).

Conclusions In PAPILLON, TTD and TTST were substantially longer for amivantamab-chemotherapy versus chemotherapy at primary analysis (cut-off on 3 May 2023). Crossover-adjusted analyses of the planned interim overall survival demonstrated a greater benefit for amivantamab-chemotherapy versus chemotherapy, further supporting amivantamab-chemotherapy as the first-line standard of care in *EGFR* exon 20 insertion-mutated non-small cell lung cancer.

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Key Points

This analysis showed that first-line amivantamab-chemotherapy substantially extended the time patients with advanced non-small cell lung cancer and with epidermal growth factor receptor (*EGFR*) exon 20 insertion stayed on treatment without the need for additional therapies compared with chemotherapy alone.

The crossover-adjusted overall survival analyses demonstrated a more pronounced and significant benefit of amivantamab-chemotherapy versus chemotherapy and provided a more clinically relevant overall survival estimate for patients treated with first-line chemotherapy consistent with real-world estimates.

These data provide further support for the durable benefit of first-line amivantamab-chemotherapy in patients with advanced non-small cell lung cancer with *EGFR* exon 20 insertion.

1 Introduction

Epidermal growth factor receptor (*EGFR*) mutations are among the most frequent mutations in non-small cell lung cancer (NSCLC) [1, 2], with exon 20 insertions (Ex20ins) representing the third most common type of *EGFR* mutation [3–5]. Amivantamab is an *EGFR*-MET bispecific antibody with immune cell-directing activity [6–8] that has shown promising anti-tumor activity across multiple NSCLC settings, including patients with *EGFR* Ex20ins [9–13]. Amivantamab monotherapy administered every 2 weeks is approved in multiple regions and countries for the treatment of *EGFR* Ex20ins-mutated NSCLC after disease progression on chemotherapy [14], and is a recommended regimen (category 2a; recommended) in the National Comprehensive Cancer Network® and European Society for Medical Oncology guidelines (category assignment pending) [15–17].

The phase III PAPILLON study evaluated amivantamab every 3 weeks after weekly administration for the first 4 weeks, in combination with the standard-of-care chemotherapy (carboplatin-pemetrexed) as a first-line (1L) treatment in participants with *EGFR* Ex20ins-mutated NSCLC [11]. At a median follow-up of 14.9 months, participants receiving amivantamab-chemotherapy had significantly longer progression-free survival (PFS) compared with chemotherapy alone (median, 11.4 months vs 6.7 months; hazard ratio [HR] 0.40 [95% confidence interval [CI] 0.30–0.53]; $p < 0.001$) [11]. Amivantamab-chemotherapy also reduced the risk of

second disease progression or death (PFS2) by 51%, with a median PFS2 that was not yet reached for amivantamab-chemotherapy versus 17.2 months for chemotherapy (HR 0.49 [95% CI 0.32–0.76]; nominal $p = 0.001$). Additionally, the planned interim overall survival (OS) analysis from the intention-to-treat (ITT) population showed a promising trend for amivantamab-chemotherapy over chemotherapy (HR 0.67 [95% CI 0.42–1.09]; $p = 0.11$) [11]. Based on these findings, amivantamab-chemotherapy has been approved in multiple regions and countries and is recommended within clinical guidelines as 1L therapy for patients with advanced *EGFR* Ex20ins-mutated NSCLC [14–21].

Before amivantamab was approved for the treatment of *EGFR* Ex20ins-mutated NSCLC after 1L chemotherapy, patients had poor prognosis, with a 12-month survival of 57%, as observed in a real-world study [22]. Because of the emerging evidence from the CHRYSALIS study demonstrating robust and durable activity for amivantamab monotherapy after chemotherapy [13], the PAPILLON study was designed to include the option for participants on the chemotherapy arm to cross over to amivantamab monotherapy every 3 weeks upon disease progression and if they met eligibility criteria for the crossover [11]. At the timing of the primary PFS analysis, 65 of 155 (42%) participants in PAPILLON crossed over per protocol from chemotherapy to amivantamab monotherapy after disease progression. The ITT-based OS in the chemotherapy arm was substantially longer than what was reported in a real-world setting where patients did not receive amivantamab [22], with a 12-month survival of 82% (95% CI 74–87), indicating that amivantamab monotherapy after chemotherapy benefited participants.

These findings support that amivantamab monotherapy may have prolonged OS in crossover participants in the PAPILLON trial. Thus, the ITT-based interim OS analysis may underestimate the long-term benefits of 1L amivantamab-chemotherapy over chemotherapy alone for clinical settings where second-line (2L) or later-line amivantamab monotherapy is not the standard of care. For this reason, an OS analysis adjusting for crossover from chemotherapy to 2L amivantamab monotherapy was warranted by estimating counterfactual survival in a setting where switching to 2L amivantamab monotherapy after 1L chemotherapy did not occur.

Additionally, time to treatment discontinuation (TTD) and time to subsequent therapy (TTST), which are other meaningful endpoints in oncology trials, are indicative of a treatment's clinical benefit. Here, TTD and TTST for amivantamab-chemotherapy versus chemotherapy, and estimates of the OS benefit for amivantamab-chemotherapy while adjusting for treatment crossover from the PAPILLON trial, are reported.

2 Materials and Methods

2.1 Study Participants

The phase III PAPILLON (ClinicalTrials.gov Identifier: NCT04538664) study enrolled participants who were 18 years of age or older and had treatment-naïve locally advanced or metastatic NSCLC with documented *EGFR* Ex20ins. Details of the study design have been previously reported [11].

2.2 Trial Design and Treatment

Participants were randomly assigned at a 1:1 ratio to receive amivantamab-chemotherapy or chemotherapy every 3 weeks on 21-day cycles. Additional details on the dosing regimens have been previously reported [11]. In accordance with the protocol, participants in the chemotherapy arm with blinded independent central review-confirmed disease progression were permitted to cross over to 2L amivantamab monotherapy (per-protocol crossover cohort). Additional eligibility criteria for the crossover cohort included not receiving anticancer or investigational therapy following discontinuation of chemotherapy and resolving all toxicities to grade ≤ 1 for severity (except for alopecia, which could be grade 2) [11]. Per protocol, all participants crossing over to 2L amivantamab monotherapy received the drug in the same dose and schedule as participants in the amivantamab-chemotherapy arm (amivantamab 1400 mg [1750 mg if ≥ 80 kg] by intravenous infusion once weekly up to cycle 2 day 1, then amivantamab 1750 mg [2100 mg if ≥ 80 kg] on day 1 of each 21-day cycle starting with cycle 3). Participants in the chemotherapy arm could not initiate treatment with 2L amivantamab monotherapy in the crossover cohort earlier than 21 days or later than 90 days after their last dose of chemotherapy, regardless of the time of disease progression.

2.3 Trial Oversight

The trial was conducted in accordance with the provisions of the Declaration of Helsinki, Good Clinical Practice guidelines (as defined by the International Council for Harmonisation), applicable regulatory requirements, and policy on bioethics and human biologic samples of the trial sponsor, Janssen Research & Development, a Johnson & Johnson company. The trial was designed by representatives of the sponsor, who were responsible for

data collection, analysis, and interpretation of trial data in collaboration with the authors.

2.4 Endpoints

The primary endpoint in PAPILLON was PFS by blinded independent central review using Response Evaluation Criteria in Solid Tumors version 1.1, which was reported previously [11]. TTST, which was one of the secondary endpoints, was defined as the time from the date of randomization to the start date of the first subsequent systemic anticancer therapy following study treatment discontinuation or death, whichever occurred first. Additional exploratory endpoints assessed included TTD (defined as the time from randomization to discontinuation of all study treatment for any reason) and crossover-adjusted OS for the chemotherapy arm. Efficacy endpoints (PFS and OS) in the crossover cohort were also evaluated [11].

2.5 Analysis

TTD and TTST were analyzed using Kaplan–Meier estimates and a Cox proportional hazards model stratified by Eastern Cooperative Oncology Group performance status (0 or 1) and history of brain metastases (yes or no). Prior *EGFR* tyrosine kinase inhibitor use was defined in the protocol as a stratification factor but was removed from the analysis because only four participants met this criterion [11].

The crossover-adjusted OS analyses were performed using the following established methods: inverse probability of censoring weighting (IPCW), two-stage estimation (TSE), and rank-preserving structural failure time (RPSFT) [23, 24]. These statistically advanced methods address bias introduced by simple adjustment methods, such as censoring crossover participants at the point of switch or excluding them entirely from the analysis, which are highly prone to selection bias as switching is likely associated with prognosis.

The IPCW method censors participants at the time of crossover and then assigns time-dependent weights to participants whose disease progressed but who did not switch to 2L amivantamab, to represent similar 2L amivantamab switchers from the time of crossover onward [23–25]. The TSE method uses a parametric survival regression model to estimate the effect of crossover by comparing post-progression survival for participants who did or did not cross over after disease progression [23, 24, 26]. IPCW and TSE rely on the “no unmeasured confounding” assumption [23–25]. The RPSFT method uses a counterfactual framework to estimate survival times that would have been observed in the absence of crossover [23, 24]. RPSFT assumes that the treatment effect in participants who crossed over is the same as in participants originally randomized to

amivantamab-chemotherapy (“common treatment effect”). More details regarding the IPCW, TSE, and RPSFT methods can be found in the Electronic Supplementary Material (ESM).

A feasibility assessment was performed to determine if sufficient data were available to conduct the crossover-adjusted analysis and to validate assumptions of the IPCW, TSE, and RPSFT methods. Sensitivity analyses were conducted for the IPCW, TSE, and RPSFT models to assess the robustness of the results under different methodologic assumptions (ESM).

Crossover-adjusted analyses of the interim OS were completed using R v4.0.4 (R Core Team, Vienna, Austria); all other analyses were completed using SAS 9.4 (SAS, Cary, NC, USA). All results reported are based on the primary analysis, which was conducted with data collected by the cutoff date of 3 May 2023.

3 Results

3.1 Participants

In total, 308 participants were randomized to amivantamab-chemotherapy ($n = 153$) or chemotherapy ($n = 155$). At the timing of the primary PFS analysis (median follow-up, 14.9 months), participants receiving amivantamab-chemotherapy had significantly longer PFS versus chemotherapy alone (HR 0.40 [95% CI 0.30–0.53]; $p < 0.001$); furthermore, 80% of participants in the amivantamab-chemotherapy arm and 72% of participants in the chemotherapy arm were still alive [11].

3.2 TTD and TTST

At the same median follow-up, 54% (83/153) of participants in the amivantamab-chemotherapy arm and 85%

Fig. 1 **a** Time to treatment discontinuation (TTD) and **b** time to subsequent therapy (TTST). ^aTTD was defined as the time from randomization to discontinuation of all study treatments for any reason. ^b TTSD was defined as the time from the date of randomization to the start date of the first subsequent systemic anticancer therapy following study treatment discontinuation or death, whichever occurred first. *CI* confidence interval, *HR* hazard ratio, *mo* months, *NE* not estimable

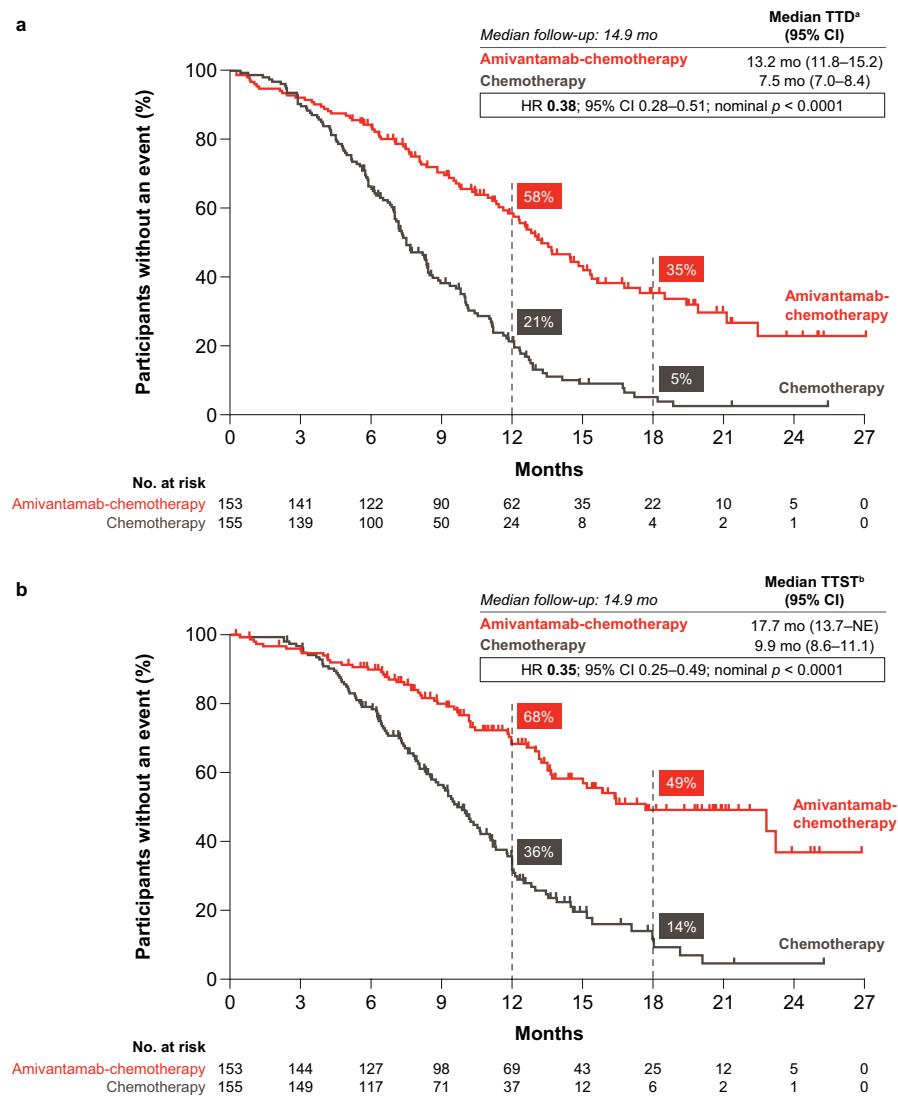


Fig. 2 Most common first subsequent systemic therapy classes. ^aThe “other” category included immuno-oncology (IO) alone and investigational agents. ^bIn the amivantamab-chemotherapy and chemotherapy arms, 23% and 1% of participants received single-agent chemotherapy, respectively, and 7% and 1% of participants received doublet chemotherapy, respectively. *EGFR* epithelial growth factor receptor, *TKI* tyrosine kinase inhibitor, *VEGFi* vascular endothelial growth factor inhibitor

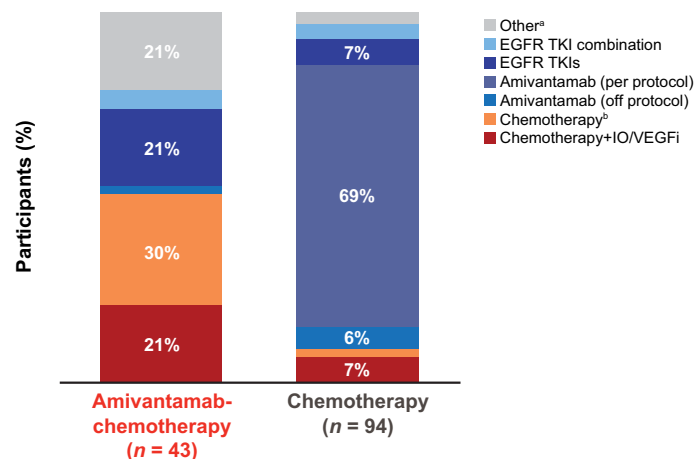


Table 1 Summary of crossover-adjusted OS

Method	OS HR (95% CI)	Setting
ITT	0.67 (0.42–1.09)	No adjustment for crossover
IPCW	0.52 (0.28–0.94)	Censor at time of crossover and reweight using stabilized weights
TSE	0.55 (0.31–0.92)	Weibull regression model without recensoring
RPSFT	0.60 (0.32–1.12)	Treatment grouping without recensoring

CI confidence interval, HR hazard ratio, IPCW inverse probability of censoring weighting, ITT intention-to-treat, OS overall survival, RPSFT rank-preserving structural failure time, TSE two-stage estimation

(131/155) of participants in the chemotherapy arm had discontinued treatment. Median TTD was 13.2 months (95% CI 11.8–15.2) in the amivantamab-chemotherapy arm and 7.5 months (95% CI 7.0–8.4) in the chemotherapy arm (HR 0.38 [95% CI 0.28–0.51]; nominal $p < 0.0001$; Fig. 1a).

In total, 28% (43/153) of participants in the amivantamab-chemotherapy arm and 61% (94/155) of participants in the chemotherapy arm went on to receive subsequent therapy. Median TTST was 17.7 months (95% CI 13.7–not estimable) in the amivantamab-chemotherapy arm and 9.9 months (95% CI 8.6–11.1) in the chemotherapy arm (HR 0.35 [95% CI 0.25–0.49]; nominal $p < 0.0001$; Fig. 1b). Among participants who received subsequent treatment after disease progression, the most common therapy in the chemotherapy arm was amivantamab monotherapy (69% as part of the per-protocol crossover cohort and 6% off protocol). The most common first subsequent therapy in the amivantamab-chemotherapy arm was chemotherapy (30%; Fig. 2). Nine participants from the amivantamab-chemotherapy arm and seven from the chemotherapy arm received a subsequent tyrosine

kinase inhibitor. No participants received a novel tyrosine kinase inhibitor, for example, sunvozertinib or zipalertinib.

3.3 Crossover-Adjusted OS

The ITT-based interim median OS analysis for amivantamab-chemotherapy versus chemotherapy was reported previously for PAPILLON (not estimable vs 24.4 months; HR 0.67 [95% CI 0.42–1.09]; Table 1) [11]. When the OS analysis was adjusted for crossover, the survival estimates in the chemotherapy arm at the median follow-up of 14.9 months were 58%, 65%, and 70% using IPCW, TSE, and RPSFT, respectively (Fig. 3). Corresponding crossover-adjusted OS HRs for amivantamab-chemotherapy versus chemotherapy were 0.52 (95% CI 0.28–0.94), 0.55 (95% CI 0.31–0.92), and 0.60 (95% CI 0.32–1.12), respectively (Table 1). Adjusted OS HR estimates were consistent across various sensitivity analyses (IPCW [HR range 0.51–0.54], TSE [HR range 0.55–0.64], and RPSFT [HR range 0.59–0.61]) performed in participants who received 2L amivantamab monotherapy per protocol ($n = 65$; Table 1 of the ESM).

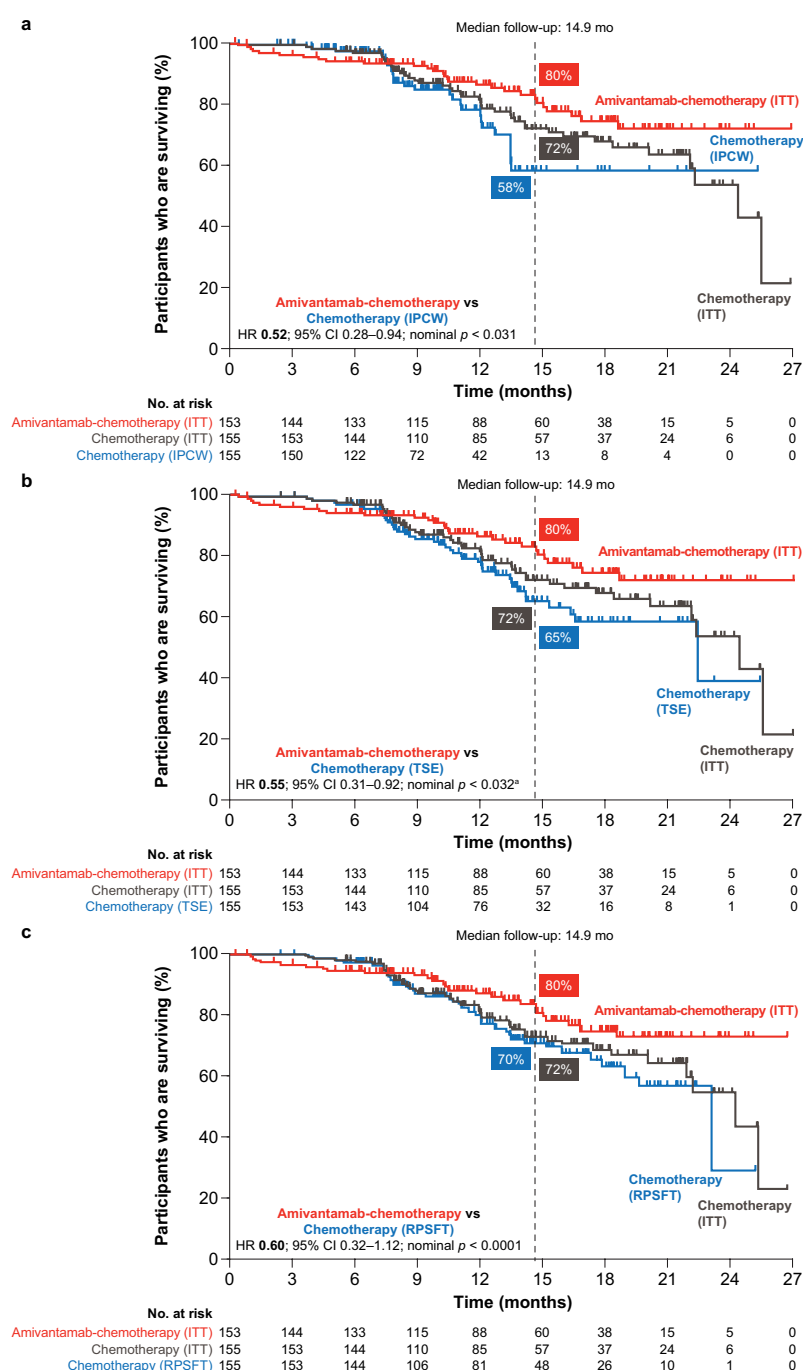
3.4 Outcomes After Crossover

Baseline characteristics, exposure to study drugs, and observed survival outcomes in the crossover cohort after 2L amivantamab monotherapy initiation are reported in the Results, Table 2, and Figs. 1 and 2 of the ESM.

4 Discussion

In the phase III PAPILLON study, participants receiving amivantamab-chemotherapy had a significant PFS benefit, a longer PFS2, and a trend toward improved OS (ITT

Fig. 3 Crossover-adjusted overall survival (OS) for **a** inverse probability of censoring weighting (IPCW), **b** two-stage estimation (TSE), and **c** rank-preserving structural failure time (RPSFT). ^a*P* value calculated by assuming log (hazard ratio [HR]) is normally distributed. *CI* confidence interval, *ITT* intention-to-treat, *mo* months



based) compared with those receiving chemotherapy alone [11]. Here, amivantamab-chemotherapy also demonstrated longer median TTD (13.2 months [95% CI 11.8–15.2] vs 7.5 months [95% CI 7.0–8.4]) and TTST (17.7 months [95% CI 13.7–not estimable] vs 9.9 months [95% CI 8.6–11.1]) compared with chemotherapy, and crossover-adjusted analyses demonstrated OS HRs that ranged from 0.52 to 0.60 compared with 0.67 per the ITT estimate.

The use of 2L amivantamab monotherapy after chemotherapy in the PAPILLON trial may have confounded the

evaluation of the full survival benefit of amivantamab-chemotherapy in the 1L setting. Crossover-adjusted OS HRs (range, 0.52–0.60) were generally consistent across the three established and validated statistical methods and a range of sensitivity analyses, demonstrating a more pronounced OS benefit compared with the ITT-based HR (0.67). Consequently, these crossover-adjusted OS HRs are less confounded by subsequent treatment differences and may be more reflective of the actual treatment benefit of 1L amivantamab-chemotherapy versus chemotherapy in

clinical settings where amivantamab monotherapy may not be available (e.g., in countries where it is not yet approved). Clinical validity of the crossover-adjusted OS analyses is further demonstrated by the similarity of the adjusted OS HRs with the OS HR of the amivantamab-chemotherapy arm in PAPILLON versus real-world 1L chemotherapy not followed by 2L amivantamab monotherapy (HR 0.48 [95% CI 0.30–0.77]) [27]. Overall, these adjusted analyses provide a clinically relevant estimate and support the robustness of the efficacy of amivantamab-chemotherapy in the 1L treatment of patients with *EGFR* Ex20ins mutations.

Crossover/treatment switching in oncology clinical trials is common, including in patient populations with NSCLC [28, 29]. It promotes an ethical design, by which participants in the control arm can receive beneficial treatment. However, crossover may interfere with the interpretation of some treatment outcomes, reinforcing the need for statistical methods to address crossover analyses [30–32]. IPCW, TSE, and RPSFT are advanced statistical methods that are recommended for adjusting OS confounding caused by crossover designs [23–25, 33, 34]. Additionally, health technology assessment agencies factor OS adjustment analyses into drug appraisals that utilize OS evidence from crossover trial designs [35]. Strengths of this analysis include that the rationale and assumptions for each externally validated adjustment method (IPCW, RPSFT, and TSE) [23, 24] were reported, and appropriate sensitivity analyses were conducted that demonstrated consistent results across a range of methods. However, each statistical approach used to estimate crossover-adjusted OS relies on assumptions that are not directly testable (e.g., common treatment effect for RPSFT and no unmeasured confounders for TSE and IPCW) [23, 24]. Nevertheless, the consistency of crossover-adjusted OS findings across multiple methodologies and statistical assumptions, and their alignment with previously published real-world estimates of 1L chemotherapy in advanced *EGFR* Ex20ins-mutated NSCLC [22, 36], support the robustness of these findings.

5 Conclusions

In the PAPILLON trial, median TTD and TTST were substantially longer in participants receiving amivantamab-chemotherapy versus chemotherapy. The crossover-adjusted OS analyses demonstrated a more pronounced benefit of amivantamab-chemotherapy over chemotherapy across multiple statistical methodologies and sensitivity analyses and provided a more clinically relevant OS estimate for patients with advanced NSCLC with *EGFR* Ex20ins who are treated with 1L amivantamab-chemotherapy. These results provide further support for the durable benefit of the use of

amivantamab-chemotherapy as the new 1L treatment regimen in advanced *EGFR* Ex20ins-mutated NSCLC.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11523-025-01182-0>.

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Declarations

Conflicts of interest Rachel E. Sanborn received honoraria from Illumina; served in a consulting or advisory role for AbbVie, Amgen, AstraZeneca, BeiGene, Boehringer Ingelheim, Curio Science, Daiichi Sankyo, GE HealthCare, Gilead, GSK, IDEology Health, Inhibrx, Eli Lilly, Johnson & Johnson, MJH Life Sciences, OncLive, Pfizer, Sanofi-Aventis, and Ose Immunotherapeutics; received research funding from Merck and AstraZeneca (investigator-sponsored trials); and received travel support to a scientific meeting from HotSpot Therapeutics. Caicun Zhou received honoraria from Eli Lilly China, Sanofi, Boehringer Ingelheim, Roche, Merck Sharp & Dohme, Qilu Pharmaceuticals, Jiangsu Hengrui Pharmaceuticals, Innovent Biologics, Alice Pharmaceuticals, C-Stone Pharmaceuticals, LUYE Pharma, TopAlliance Biosciences Inc., Amoy Diagnostics, and AnHeart Therapeutics; and served in a consulting or advisory role for Innovent Biologics, Qilu Pharmaceuticals, Jiangsu Hengrui Pharmaceuticals, and TopAlliance Biosciences Inc. Ke-Jing Tang has no conflicts of interest that are directly relevant to the content of this article. Byoung Chul Cho received research funding from AstraZeneca, Champions Oncology, CJ Bioscience, Johnson & Johnson, Merck Sharp & Dohme, Dong-A ST, Yuhan Corporation, ImmuneOncia, Therapex, J INTS BIO, Vertical Bio AG, GI Innovation, and Cyrus Therapeutics; received royalties or licenses from Champions Oncology, Crown Bioscience, Imagen, and PearlRiver Bio GmbH; served in a consulting or advisory role for BeiGene, Novartis, AstraZeneca, Boehringer Ingelheim, Roche, Bristol Myers Squibb, CJ Bioscience, Cyrus Therapeutics, Ono Pharmaceutical, Yuhan Corporation, Pfizer, Eli Lilly, Guardant Health, Takeda, Merck Sharp & Dohme, Janssen, Gilead, Amgen, Daiichi Sankyo, Regeneron, Sanofi, AnHeart Therapeutics, Seagen, Harpoon Therapeutics, GSK, ArriVent Biopharma, BridgeBio, Kanaph Therapeutics, Cyrus Therapeutics, J INTS BIO, and Therapex; served in a leadership role for J INTS BIO; has stock ownership or other ownership interests with Theravance, Gencurix, BridgeBio, Kanaph Therapeutics, Cyrus Therapeutics, Interpark Bio, Convergence Corp, and J INTS BIO; reports employment with Yonsei University Health System; and other relationships with DAAN Biotherapeutics. Susanne Cheng served in an advisory role for Merck and AstraZeneca. Sanjay Popat served on advisory boards for Boehringer Ingelheim, Novartis, Amgen, Johnson & Johnson, Daiichi Sankyo, AstraZeneca, Bayer, Bristol Myers Squibb, Blueprint Medicines, Merck Serono, Guardant Health, BeiGene, Takeda, Eli Lilly, Roche, Turning Point Therapeutics, GSK, Merck Sharp & Dohme, Pfizer, Sanofi, and EQRx; served as an invited speaker for Medscape and VJOncology; has other relationships with Elsevier, Amgen, Merck Sharp & Dohme, and Blueprint Medicines; served as a coordinating PI for ARIAD Pharmaceuticals, Boehringer Ingelheim, Celgene, Takeda, Turning Point Therapeutics, Roche, Johnson & Johnson, Bristol Myers Squibb, and Eli Lilly; served as a local PI for AstraZeneca, Roche, GSK, and Trizell; received research grants from Guardant Health; served in a leadership role for the British Thoracic Oncology Group and European Thoracic Oncology Platform; served in an advisory role for ALK Positive UK, International Association for

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Ethics approval The trial was conducted in accordance with the provisions of the Declaration of Helsinki, Good Clinical Practice guidelines (as defined by the International Council for Harmonisation), applicable regulatory requirements, and the policy on bioethics and human biologic samples of the trial sponsor, Janssen Research and Development. The study protocols, amendments, and relevant documents were approved by the local independent ethics committee or institutional review board at each study site.

Consent to participate All patients provided written informed consent prior to treatment.

Consent for publication Not applicable.

Availability of data and material The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at <https://www.janssen.com/clinical-trials/transparency>. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at <http://yoda.yale.edu>.

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- ²⁶ MD Anderson Cancer Center, Houston, TX, USA
- ²⁷ Johnson & Johnson, Wayne, PA, USA
- ²⁸ Janssen-Cilag Ltd, a Johnson & Johnson company, High Wycombe, UK
- ²⁹ Janssen Pharmaceutica NV, a Johnson & Johnson company, Beerse, Belgium
- ³⁰ Johnson & Johnson, Mumbai, India
- ³¹ Evidera, Waltham, MA, USA
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