Stable disease (SD) on amivantamab in post-platinum epidermal growth factor receptor (EGFR) exon 20 insertion (ex20ins) mutated non-small cell lung cancer (NSCLC): A response-based analysis

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INTRODUCTION

- NSCLC harboring epidermal growth factor receptor (EGFR) exon 20 insertion mutations (ex20ins) has been associated with poor prognosis, especially after progression on standard-of-care, platinum-based chemotherapy[1-4]
- Amivantamab—an EGFR-MET bispecific antibody—was the first targeted therapy approved for this patient population[5, 6]
- As antitumor activity in single-arm studies typically focuses on complete response and partial response (PR), and the duration of these responses, we sought to characterize the clinical benefit observed in patients who experienced stable disease (SD) as best response

OBJECTIVE

- A landmark analysis was performed to assess outcomes in patients with EGFR ex20ins NSCLC from the CHRYSALIS study who achieved SD as best response and did not progress on amivantamab at 12 weeks of treatment

METHODS

- This response-based analysis included 114 patients with ex20ins NSCLC whose disease progressed on or after platinum-based chemotherapy and who received the approved dose of amivantamab (1050 mg, <80 kg; 1400 mg, ≥80 kg) on or before 4 June 2020 in the CHRYSALIS study (NCT02609776; data cut-off: 30 March 2021)
- In CHRYSALIS, amivantamab demonstrated an overall response rate (by blinded independent central review [BICR]) of 43% and a median duration of response of 10.8 months, median (95% confidence intervals [CI]) progression-free survival (PFS) of 6.74 (5.45, 9.66) months, and median (95% CI) overall survival (OS) of 22.77 (17.48, not evaluable [NE]) months among these 114 patients, which is consistent with an earlier report[7]
- Response was assessed by BICR using RECIST v1.1
- Patients alive and evaluable at the 12-week treatment landmark were grouped by response observed at 12 weeks (best response of PR or better [PR+] or SD if progression-free at landmark; or progressive disease [PD])
- PFS and OS by responder cohort were estimated using the Kaplan–Meier method
  - Patients who achieved PR+ or SD were included in PFS and OS analyses; patients with PD were only included in the OS analysis
- Hazard ratios (HRs) and 95% CIs between response cohorts were estimated using Cox proportional hazards regression

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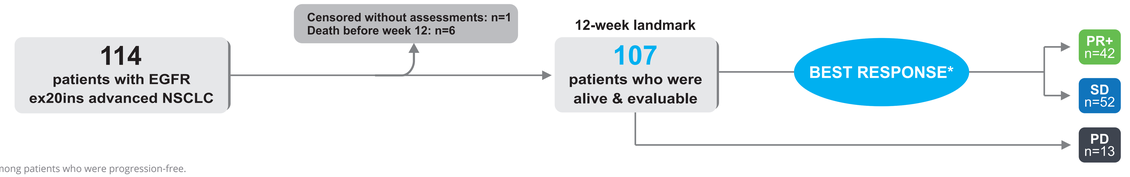
RESULTS

- Overall, 107 of the 114 patients were alive and evaluable at week 12: 42 (39%) with PR+, 52 (49%) with SD, and 13 (12%) with PD (**Figure 1**)

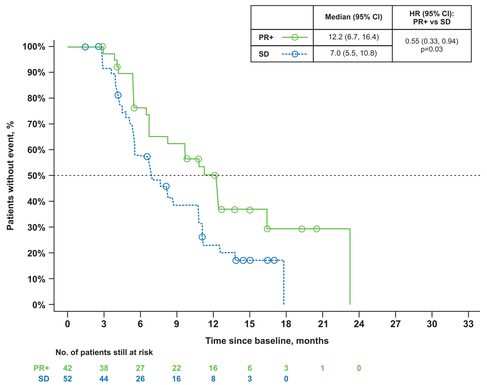
Figure 1. Patient disposition



*Among patients who were progression-free.

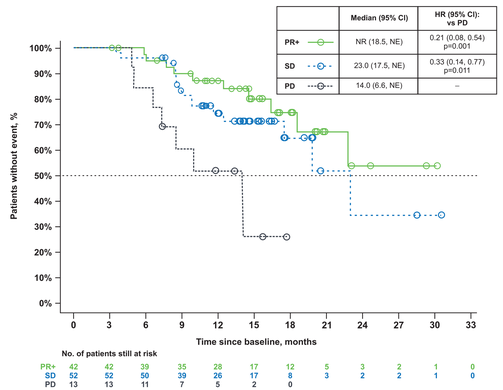
- Patients who achieved PR+ or SD had a median (95% CI) PFS of 12.2 (6.7, 16.4) months and 7.0 (5.5, 10.8) months, respectively (HR [PR+ vs SD]=0.55 [95% CI: 0.33, 0.94]; p=0.03; **Figure 2**)
- Patients with PR+ or SD had significant reductions in risk rate of death: HR of PR+ vs PD=0.21 (95% CI: 0.08, 0.54); p=0.001 and HR of SD vs PD=0.33 (95% CI: 0.14–0.77); p=0.011 (**Figure 3**)

Figure 2: Progression-free survival for patients alive at 12 weeks*



*Only patients progression-free and alive at 12 weeks.

Figure 3. Overall survival by best response*



*Patients alive at 12 weeks; patients who progressed after response were assigned to the PD group.

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KEY TAKEWAY

Clinically meaningful improvement in disease control and OS was achieved with amivantamab, even in patients with EGFR ex20ins advanced NSCLC whose depth of tumor response did not meet RECIST 1.1-defined response

CONCLUSIONS

Treatment benefit with amivantamab was observed in patients who achieved SD, in addition to those who achieved PR+, as best response

Patients with EGFR ex20ins advanced NSCLC who achieved PR+ and SD had 79% and 67% reductions in risk rate of death, respectively, versus patients with PD

Findings demonstrate the value of disease control, regardless of depth of response, with amivantamab

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DISCLOSURES

N. Girard: Financial Interests, Personal, Research Grant: AstraZeneca, AbbVie, Amgen, Boehringer-Ingelheim, Eli Lilly, Hoffmann-La Roche, Janssen, Merck, MSD, Novartis, Pfizer, Sivan, and Trizell; Financial Interests, Personal, Advisory Role: Bristol Myers Squibb, AstraZeneca, AbbVie, Amgen, Boehringer Ingelheim, Eli Lilly, Hoffmann-La Roche, Janssen, Merck, MSD, Novartis, Pfizer, Sanofi, and Sivan; Financial Interests, Personal, Full or part-time Employment, Family member: AstraZeneca. **K. Park:** Financial Interests, Personal, Advisory Role: AstraZeneca, Lilly, Ono Pharmaceutical, Bristol Myers Squibb, MSD, Blueprint Medicines, Amgen, Merck KGaA, LOXO, AbbVie, Daiichi Sankyo, Boehringer Ingelheim, JNJ, Eisai, Puma Biotechnology; Financial Interests, Personal, Speaker's Bureau: Boehringer Ingelheim; Financial Interests, Personal, Research Grant: AstraZeneca, MSD Oncology. **S. Viteri:** Financial Interests, Personal, Advisory Role: AbbVie, Bristol Myers Squibb, Roche, Takeda, AstraZeneca, and MSD; Financial Interests, Personal, Speaker's Bureau: Bristol Myers Squibb, MSD, Roche, AstraZeneca; Financial Interests, Personal, Other, Travel Expenses: Roche, OSE Pharma, Bristol Myers Squibb, Merck, Merck Serono, Puma Biotechnology, and Janssen Cilag. **C.A. Schioppa, J. Diels, M. Oguz, B.H. Rodrigues, N. Rahhali, J. Sermon, F. Ghilotti, T. Li, R.E. Knoblauch, P. Mahadevia:** Financial Interests, Personal, Full or part-time Employment: Johnson & Johnson; Financial Interests, Personal, Stocks/Shares: Johnson & Johnson. B.C. Cho: Financial Interests, Personal, Research Grant: Novartis, Bayer, AstraZeneca, MOGAM Institute, Dong-A ST, Champions Oncology, Janssen, Yuhan, Ono, Dizal Pharma, MSD, Abbvie, Medpacto, GInnovation, Eli Lilly, Blueprint medicines, Interpark Bio Convergence Corp; Financial Interests, Personal, Advisory Role: Novartis, AstraZeneca, Boehringer-Ingelheim, Roche, BMS, Ono, Yuhan, Pfizer, Eli Lilly, Janssen, Takeda, MSD, Medpacto, Blueprint medicines; Financial Interests, Personal, Stocks/Shares: TheraCanVac Inc, Gencurix Inc, Bridgebio therapeutics, KANAPH Therapeutic Inc, Cyrus therapeutics, Interpark Bio Convergence Corp.; Financial Interests, Personal, Advisory Board: KANAPH Therapeutic Inc, Brigebio therapeutics, Cyrus therapeutics, Guardant Health, Joseph BIO; Financial Interests, Personal, Member of the Board of Directors: Gencurix Inc, Interpark Bio Convergence Corp.; Financial Interests, Personal, Royalties: Champions Oncology; Financial Interests, Personal, Other, Founder: DAAN Biotherapeutics.