Crossover Adjusted Overall Survival for Amivantamab (AM) Plus Chemotherapy vs Chemotherapy in First-line *EGFR* Exon 20 Insertion NSCLC

Shun Lu, Caicun Zhou, Byoung Chul Cho, Akira Ono, Hidetoshi Hayashi, Margarita Majem, Se-Hoon Lee, Gary Richardson, Joshua K Sabari, Nicolas Girard, Rachel E Sanborn, Aaron S Mansfield, Nasuh Buyukkaramikli, Nolen Perualila, Sandip Acharya, Conor Chandler, Lindsay Dearden, Trishala Agrawal, Mahadi Baig, Keunchil Park[19]

Background

In approximately 10% of EGFR-mutated NSCLC, EGFR is activated through one of a group of heterogenous, in-frame base pair insertions in EGFR Exon 20, collectively referred to as EGFR Exon 20ins mutations. NSCLC arising from Exon 20ins mutations is distinguished by de novo resistance to currently approved EGFR TKIs, including third-generation TKIs such as osimertinib. In the absence of effective targeted therapies, platinum-based doublet chemotherapy remains the standard of care. The efficacy of combination chemotherapy in patients with advanced NSCLC and EGFR L858R or Exon 19del mutations includes an objective response rate (ORR) of approximately 30% and median PFS of approximately 5 months. Amivantamab is being developed based on the hypothesis that a bispecific antibody, by targeting the extracellular domain of each receptor (EGFR and MET), will demonstrate activity against tumors resistant to EGFR TKIs, either through primary resistance (EGFR Exon 20ins) or through the two most frequent mechanisms of resistance to current EGFR therapies: 1) secondary/tertiary mutations in EGFR, and 2) MET amplification or mutation.

Aim

Primary

To compare the efficacy, as demonstrated by PFS, in participants treated with AM in combination with chemotherapy, versus chemotherapy alone

Secondary

To further assess the clinical benefit achieved with AM in combination with chemotherapy, versus chemotherapy alone

To assess the safety in participants treated with AM in combination with chemotherapy, versus chemotherapy alone

To assess the relationship between pharmacokinetics or immunogenicity and selected endpoints (including but not limited to efficacy, safety and/or PRO

To assess health-related quality of life and disease-related symptoms in participants treated with AM in combination with chemotherapy, versus chemotherapy alone

Method

Phase 3 study evaluating the efficacy of 1L amivantamab-chemotherapy vs chemotherapy in patients with advanced NSCLC with *EGFR* Ex20ins

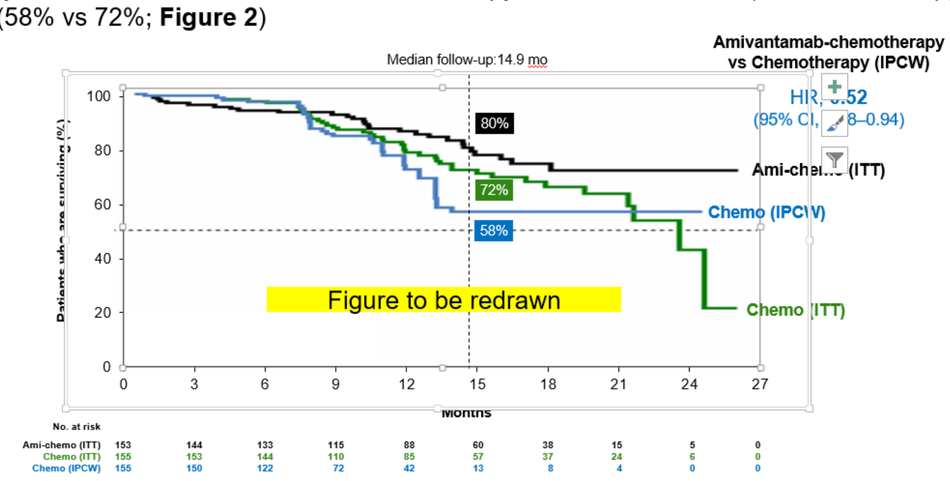
Patients in the chemotherapy arm with BICR-confirmed disease progression using RECIST v1.1 were permitted to crossover to 2L amivantamab monotherapy

This analysis estimated adjusted OS HR for amivantamab-chemotherapy vs chemotherapy in the absence of 2L amivantamab

Results

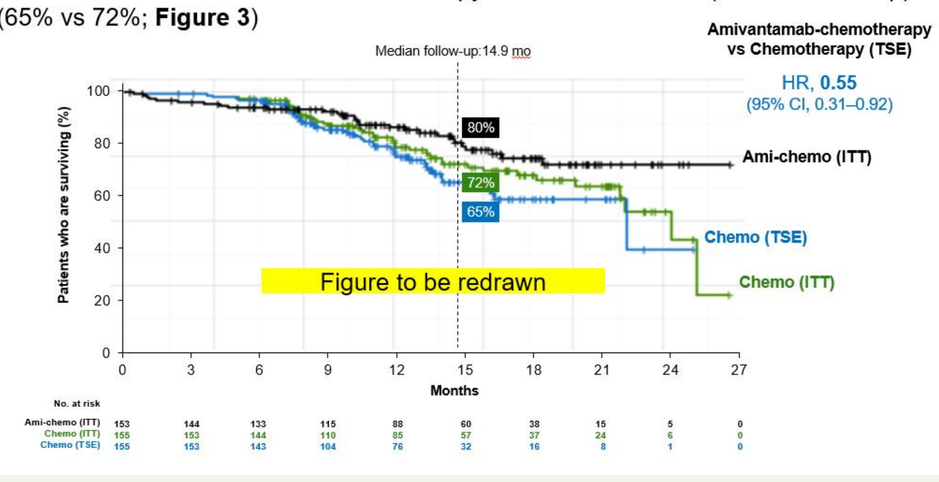
Survival before Cross-over

- The IPCW-adjusted survival estimate for the chemotherapy arm at 14.9 months (median follow-up) was lower than the ITT (58% vs 72%; **Figure 2**)



Survival after Cross-over

- The TSE-adjusted survival estimate for the chemotherapy arm at 14.9 months (median follow-up) was lower than the ITT (65% vs 72%; **Figure 3**)



Conclusion

1L amivantamab-chemotherapy demonstrated significantly improved outcomes compared to chemotherapy in patients with *EGFR* Ex20ins-mutated NSCLC in PAPILLON

The interim ITT OS analysis included 65 patients who crossed over from chemotherapy to 2L amivantamab monotherapy

At the median follow-up (14.9 months), the crossover-adjusted OS analyses suggest that ITT OS may underestimate the survival benefit of 1L amivantamab-chemotherapy (OS HR: ITT, 0.67; IPCW, TSE, and RPSFT, 0.52–0.60)