Amivantamab-chemotherapy in NSCLC with *EGFR* exon 20 insertions: Treatment crossover analysis from PAPILLON

Rachel E. Sanborn, Caicun Zhou, Ke-Jing Tang, Byoung Chul Cho, Susanna Cheng, Sanjay Popat, Akira Ono, Shun Lu, Margarita Majem, Andres Aguilar, Maria Del Rosario Garcia Campelo, Hidetoshi Hayashi, MD, Kang-yun Lee, Se-Hoon Lee,, Angelo Delmonte, Jorge Arturo Alatorre, Gary Richardson, Victor Santos , Christophe Dooms, MD, PhD Joshua K. Sabari, Catherine A. Shu, MD, Nicolas Girard, Aaron S. Mansfield, Keunchil Park, Yichuan Xia, Archan Bhattacharya, Nasuh Buyukkaramikli, Nolen Perualila, Joris Diels, Sandip Acharya, Conor Chandler, Irina Proskorovsky, Lindsay Dearden, Honeylet Wortman-Vayn, Parthiv J. Mahadevia, Roland E. Knoblauch, Trishala Agrawal, Mahadi Baig, Enriqueta Felip·

Background

In PAPILLON, first-line amivantamab-chemotherapy in epidermal growth factor receptor (*EGFR)* exon 20 insertion–mutated non-small-cell lung cancer (NSCLC) demonstrated significantly prolonged progression-free survival and favorable overall survival over chemotherapy; consistent benefit was observed with secondary endpoints. Nevertheless, overall survival in the intention-to-treat population may underestimate the clinical benefit of amivantamab-chemotherapy because 65/155 participants crossed over per-protocol from chemotherapy to amivantamab monotherapy. Therefore, intention-to-treat–based comparisons may not fully reflect the survival advantage of amivantamab-chemotherapy for appropriate clinical application.

Method

Intravenous amivantamab was administered weekly for the first 4 weeks (1400 mg; ≥80 kg, 1750 mg) and every 3 weeks from Week 7 (1750 mg; ≥80 kg, 2100 mg). Carboplatin (area under curve 5 mg/mL/min) was administered for 4 cycles. Pemetrexed (500 mg/m^2) was administered until disease progression. Time to treatment discontinuation and time to subsequent therapy were evaluated. Crossover-adjusted survival estimates were generated using established statistical methods.

Results

From December 2020 to November 2022, 308 participants with treatment-naive, *EGFR* exon 20 insertion–mutated NSCLC were randomized (amivantamab-chemotherapy, n=153; chemotherapy, n=155). At a median follow-up of 14.9 months, median time to treatment discontinuation was 13.2 versus 7.5 months for amivantamab-chemotherapy versus chemotherapy, respectively (hazard ratio, 0.38 [95% CI, 0.28-0.51]; nominal *P*<0.0001). Median time to subsequent therapy was 17.7 versus 9.9 months (hazard ratio, 0.35 [95% CI, 0.25-0.49]; nominal *P*<0.0001). Compared with the intention-to-treat estimate (hazard ratio, 0.67 [95% CI, 0.42-1.09]), crossover-adjusted overall survival analyses demonstrated a more favorable benefit for amivantamab-chemotherapy versus chemotherapy, with hazard ratios ranging from 0.52 to 0.60.

Conclusion

Time to treatment discontinuation and subsequent therapy were substantially longer for amivantamab-chemotherapy versus chemotherapy. Crossover-adjusted overall survival analyses demonstrated a greater survival benefit for amivantamab-chemotherapy versus chemotherapy, further supporting amivantamab-chemotherapy as the first-line standard-of-care in *EGFR* exon 20 insertion–mutated NSCLC.

Cabrini RESEARCH