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Amivantamab (JNJ-61186372), an EGFR-MET bispecific antibody, in combination with lazertinib, a 3rd-generation tyrosine kinase inhibitor (TKI), in advanced EGFR NSCLC

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Background

In preclinical studies, the combination of amivantamab (EGFR-MET bispecific antibody) with lazertinib demonstrates synergistic inhibition of tumor growth. We present the safety and early efficacy results of patients receiving amivantamab in combination with lazertinib in the phase 1 CHRYSALIS study (NCT02609776).

Methods

Patients with EGFR Exon 19 deletion or L858R mutation non-small cell lung cancer (NSCLC) were enrolled in this 2-part study. To identify the recommended phase 2 combination dose (RP2CD), Part 1 enrolled patients without restriction on prior therapy to evaluate escalating dose cohorts of amivantamab (700–1050 mg, iv once weekly for 28 days; biweekly thereafter) in combination with standard monotherapy dosing of lazertinib (240 mg oral daily). The ongoing Part 2 dose expansion Cohort E is evaluating preliminary efficacy, without biomarker selection, in patients progressing on osimertinib. Response was assessed by investigator per RECIST v1.1.

Results

As of 17 March 2020, 71 patients received the combination: median age was 61 y (36–79), median prior lines was 1 (0–9). In Part 1, the RP2CD was the maximally assessed doses of 1050 mg (1400 mg, ≥80 kg) amivantamab + 240 mg lazertinib. Interim safety profile includes rash (78%), infusion related reaction (61%), paronychia (42%), stomatitis (31%), pruritus (24%), and diarrhea (14%). Majority of treatment-related AEs were grade 1–2, with grade ≥3 reported in 7%. As of 30 April 2020, in 23 Part 1 patients with measurable disease, the overall response rate (ORR) was 43.5% (95% CI, 23.2–65.5) with 10 partial responses (PRs), and 9 patients with stable disease (SD); median treatment duration was 8.2 months (0.5–10.7), with 13 patients still ongoing. In the post-osimertinib expansion Cohort E, early antitumor activity is being observed in 14/20 response-evaluable patients with 1 complete response, 7 PRs (2 pending confirmation), and 6 SD with tumor shrinkage.

Conclusions

Amivantamab can be combined safely with lazertinib at their respective full monotherapy doses. Encouraging preliminary activity was observed in osimertinib-relapsed disease: updated data will be presented.

Clinical trial identification

NCT02609776; submitted November 18, 2015.

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Disclosure

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