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Updated overall survival analysis from the phase II PHAROS study of encorafenib plus binimetinib in patients with BRAF V600E-mutant metastatic NSCLC (mNSCLC)

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Background

The combination of encorafenib (enco; BRAF inhibitor) and binimetinib (bini; MEK inhibitor) showed meaningful clinical benefit and a manageable safety profile in the phase II PHAROS study (NCT03915951) in treatment-naïve and previously treated patients (pts) with BRAF V600E-mutant mNSCLC. Median progression-free survival was 30.2 mo in treatment-naïve and 9.3 mo in previously treated pts; median overall survival (mOS) was not reached and 22.7 mo (95% CI, 14.1, 32.2), respectively. We report results from an updated OS analysis.

Methods

PHAROS, an ongoing open-label, single-arm, phase II study, enrolled 98 pts with BRAF V600E-mutant mNSCLC who were treatment-naïve or had received 1 prior systemic therapy. Pts received enco 450 mg once daily and bini 45 mg twice daily. Primary endpoint was objective response rate; secondary endpoints included OS and safety.

Results

At data cutoff (Mar 14, 2025), 5 of 59 treatment-naïve (8%) and 3 of 39 previously treated pts (8%) were still receiving enco+bini. After median follow-up for OS of 52.3 mo (95% CI, 46.8, 58.3) in treatment-naïve pts, 30 events occurred and mOS was 47.6 mo (95% CI, 31.3, not estimable [NE]); the 4-year OS rate was 49% (95% CI, 35, 62). After median follow-up for OS of 48.2 mo (95% CI, 41.6, 57.4) in previously treated pts, 23 events occurred and mOS was 22.7 mo (95% CI, 14.1, 32.6); the 4-year OS rate was 31% (95% CI, 16, 47). Safety profile remained consistent with that in prior analyses, with the most common treatment-related adverse events being nausea (52%), diarrhea (44%), fatigue (33%), and vomiting (30%). In treatment-naïve and previously treated pt cohorts, 58% and 26% received ≥1 subsequent anticancer systemic treatment, respectively; of those pts, 68% and 50% received ≥1 subsequent PD-(L)1 treatment, and 38% and 30% received ≥1 subsequent BRAF ± MEK inhibitor, respectively.

Conclusions

In this analysis after a median of approximately 4 years of follow-up, enco+bini showed prolonged mOS of approximately 4 years in treatment-naïve pts, which is the longest mOS reported to date with targeted therapies in this patient population from pivotal trials. Long-term safety was consistent with prior analyses, with no new safety signals observed.

Clinical trial identification

NCT03915951.

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