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Phase II study of belzutifan (MK-6482), an oral hypoxia-inducible factor 2α (HIF-2α) inhibitor, plus cabozantinib for treatment of advanced clear cell renal cell carcinoma (ccRCC)

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Background

Belzutifan monotherapy has shown antitumor activity and favorable safety in advanced ccRCC. This ongoing, open-label, phase II study (NCT03634540) investigates belzutifan plus cabozantinib for pts with advanced ccRCC who were either treatment naive (cohort 1) or previously treated with immunotherapy (cohort 2). This analysis presents data from cohort 2.

Methods

Pts had advanced ccRCC and had previously received immunotherapy and ≤2 systemic treatment regimens. Initially, a safety review committee evaluated the first 6 pts enrolled in either cohort for 21 days to determine the recommended phase II dose (RP2D). The primary end point was ORR (CR + PR) per RECIST v1.1 by investigator review. Secondary end points were DCR (CR + PR + SD), DOR, PFS, and OS. For this preliminary analysis, efficacy was evaluated in pts who received ≥1 dose of treatment and had an opportunity for ≥6 mo of follow-up. Safety was evaluated in all pts.

Results

In the first 6 pts enrolled, 1 had a DLT (hand–foot syndrome); belzutifan 120 mg plus cabozantinib 60 mg was determined to be the RP2D. Overall, 52 pts were enrolled in cohort 2 and were included in the safety analysis set. In all pts, 28 (54%) previously received 1 line therapy and 24 (46%) previously received 2 lines of therapy. Median time from enrollment to data cutoff was 8.9 mo (range, 2.2-24.0). In the efficacy analysis set (N = 41), ORR was 22% (9 PRs) and DCR was 90%; 88% of pts had tumor shrinkage. Median DOR was not reached (range, 3.7+ to 14.8+ mo); all responses were ongoing as of the data cutoff date. Median PFS was 16.8 mo (95% CI, 9.2 to not reached); PFS rate at 12 mo was 65%; OS rate at 12 mo was 81%. In all pts, 98% had a treatment-related adverse event (TRAE); most events (92%) were grade 1 or 2. Incidence of grade 3 TRAEs ≥10% were hypertension (23%), anemia (12%), and fatigue (12%). Two (4%) pts experienced grade 3 hypoxia. There were no grade 4 or 5 TRAEs. Discontinuations owing to TRAEs occurred in 6 pts (12%) for belzutifan and 8 pts (15%) for cabozantinib.

Conclusions

In this preliminary analysis, belzutifan plus cabozantinib had manageable safety and showed promising antitumor activity in previously treated pts with advanced ccRCC.

Clinical trial identification

NCT03634540, August 16, 2018.

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Legal entity responsible for the study

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