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A phase II prospective trial of frontline cabozantinib in metastatic collecting ducts renal cell carcinoma: The BONSAI trial (Meeturo 2)

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Background

Metastatic collecting ducts carcinoma (mCDC) is biologically poorly characterized and under-represented in prospective randomized trials.

Methods

This prospective, monocentric, phase II trial tested cabozantinib (cabo) 60 mg in treatment-naïve mCDC patients (pts). Primary endpoint was objective response rate (ORR) per RECIST 1.1. Secondary endpoints were progression-free survival (PFS), overall survival and safety profile. Exploratory objectives were: to identify somatic mutations by targeted DNA sequencing; to define molecular subtypes, signatures and transcript fusions genes by RNA sequencing. A central pathological review was mandatory. The study was based on a Simon's two-stage optimal design.

Results

From January 2018 to November 2020, 25 pts were enrolled, of whom 23 started treatment. Median age was 66 years, 19 pts were male. The most common metastatic sites were lymph nodes and bone (15 and 13 pts), followed by lung and liver (10 and 4 pts). Median follow up was 8 months. ORR was 35% (1 CR and 7 PR). Median PFS was 6 months. All pts reported at least one grade (G) 1-2 adverse event (AE): the most common were fatigue (43%), hypothyroidism (28%), stomatitis (28%), anorexia (26%), hand-foot syndrome (13%), hypertension (17%), and diarrhea (13%). Five pts reported G3 AEs (2 thromboembolic events, 2 arterial hypertension, 1 fatigue), while no G4-5 AEs were reported. 17% of pts required dose reduction. DNA sequencing was successful in 21 (91%) patients. All tumors were microsatellite stable. No association between tumor mutational burden and response to cabo was observed. The most affected pathways were chromatin-modifying enzymes (46%) and adaptive immune system (23%). Responsive pts (PFS > 6 months) showed high frequency of mutations affecting deubiquitination, cell-cell communication, and TGF-b signaling. Non-responders were frequently mutated in chromatin remodeling, transcriptional regulation and WNT pathways.

Conclusions

The study met its primary endpoint showing promising efficacy and acceptable tolerability of cabo in mCDC pts. Mature results according to mutational profiles and gene signatures will be presented.

Clinical trial identification

NCT03354884.

Legal entity responsible for the study

The authors.

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Disclosure

All authors have declared no conflicts of interest.