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Cabozantinib (C) in combination with atezolizumab (A) as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Results from the COSMIC-021 study

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Background

C, a standard-of-care for treatment of advanced RCC, promotes an immune-permissive environment which may enhance response to immune checkpoint inhibitors. COSMIC-021, a multicenter phase 1b study, is evaluating the combination of C + A in various solid tumors (NCT03170960). We present initial results in first-line ccRCC.

Methods

Patients (pts) with ccRCC were enrolled in the dose escalation (N=10) and expansion stage (N=60). Pts were enrolled sequentially to receive A 1200 mg IV Q3W with either C 40 mg (dose level 40 [DL_{40}], N=34) or C 60 mg (DL_{60}, N=36) PO QD in each stage. Eligible pts had ECOG PS 0-1. None had received prior systemic anticancer therapy for advanced RCC. The primary endpoint is ORR per RECIST v1.1 by investigator. Other endpoints include safety, PFS, and OS.

Results

As of Mar 27, 2020, 70 pts with ccRCC (34 at DL_{40} and 36 at DL_{60}) had a median follow-up of 22.0 mo (range 17, 29) for DL_{40} and 11.5 (6, 28) for DL_{60}. Baseline characteristics were similar in the two dose groups. Median age for all pts was 65 y, 76% were male, 74% had ECOG PS 0, 87% had prior nephrectomy, 77% had lung metastases, and 46% had ≥3 sites of disease. 30% were favorable, 67% were intermediate, and 3% were poor risk by IMDC criteria. Grade 3/4 TRAEs occurred in 71% of DL_{40} and 64% of DL_{60} pts, with no grade 5 TRAEs at either dose. The most common grade 3/4 TRAEs in all pts were hypertension (21% in DL_{40} and 14% in DL_{60}), diarrhea (9% and 19%), hypophosphatemia (15% and 3%), and ALT increased (3% and 14%). For DL_{40}, ORR was 47% (1 CR and 15 PRs), DCR (CR+PR+SD) was 94%, median PFS was 19.5 mo, and 12 mo PFS rate was 67%. For DL_{60}, ORR was 58% (2 CRs and 19 PRs), DCR was 92%, median PFS was 20.4 mo, and 12 mo PFS rate was 71%. Available tumor tissue (n=40) was evaluated for PD-L1 expression, and no association with antitumor activity was shown. Increased median levels of activated peripheral cytotoxic T (+8%) and NK (+24%) cells were observed at day 21 with a concomitant decrease in immunosuppressive cells.

Conclusions

C + A demonstrated encouraging clinical activity in previously untreated pts with advanced ccRCC with an acceptable safety profile at both C doses evaluated. A phase 3 study of C + A in RCC previously treated with ICI therapy is planned.

Clinical trial identification

NCT03170960.

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Legal entity responsible for the study

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Disclosure

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