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Cabozantinib (C) in combination with atezolizumab (A) in non-clear cell renal cell carcinoma (nccRCC): Results from cohort 10 of the COSMIC-021 study

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Background

NccRCC encompasses a heterogenous group of histologies comprising ⊠25% of all RCC diagnoses with worse outcomes than ccRCC. Both C monotherapy and immune checkpoint inhibitors (ICIs) have shown preliminary activity in nccRCC, and several phase 2 trials are evaluating C in nccRCC. C promotes an immune-permissive environment which may enhance response to ICIs and has shown encouraging activity in combination with ICIs in tumor types including ccRCC, UC, mCRPC , and HCC. COSMIC-021, a multicenter phase 1b study, is evaluating the combination of C with A in various solid tumors (NCT03170960). We report initial results from cohort 10 in nccRCC.

Methods

Eligible patients (pts) had ECOG PS 0-1 and had received ≤1 prior VEGFR-TKI therapy for advanced nccRCC. Prior ICI or C therapy was not allowed. Pts received C 40 mg PO QD and A 1200 mg IV Q3W. The primary endpoint is objective response rate (ORR) per RECIST v1.1 by investigator. Other endpoints include safety, duration of response (DOR), PFS, and OS.

Results

As of Mar 27, 2020, 30 pts were enrolled with a median follow-up of 9.2 mo (range 4, 16); histological subtypes were papillary, n=15; chromophobe, n=7; and other, n=8. Median age was 61 y, 87% were male, 70% had ECOG PS 0, 80% had prior nephrectomy, and 57% had ≥3 sites of disease. Five pts (17%) had received prior VEGFR-TKI therapy (two in combination with everolimus). 37% were favorable, 50% were intermediate, and 13% were poor risk by IMDC criteria. Grade 3/4 TRAEs occurred in 30%, with no grade 5 TRAEs. Hypophosphatemia was the most common grade 3/4 TRAE (4 [13%]). Confirmed ORR per RECIST v1.1 was 33%; ten pts had PRs (papillary, n=6; chromophobe, n=1; ccRCC, n=1; translocation, n=1; and unclassified, n=1). Responses occurred in all IMDC risk groups. DCR (CR+PR+SD) was 93%. Median DOR was 7.9 mo (range 1.0+, 8.3+). Increased median levels of activated peripheral cytotoxic T (+13%) and NK (+34%) cells were observed at day 21 with a concomitant decrease in immunosuppressive cells.

Conclusions

C + A demonstrated encouraging clinical activity in pts with nccRCC with an acceptable safety profile. Responses were observed in multiple histologies. Antitumor immunomodulatory effects were observed in peripheral blood with C + A.

Clinical trial identification

NCT03170960.

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Legal entity responsible for the study

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Disclosure

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