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Efficacy of cabozantinib and nivolumab in cluster 1/2 metastatic clear cell renal cell carcinoma: Results from OPTIC RCC, a phase II trial of a novel RNAseq-based biomarker

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Background

First-line treatment of metastatic clear cell renal cell carcinoma (mccRCC) includes a PD-1 inhibitor plus an anti-CTLA-4 antibody (IO/IO) or an anti-vascular endothelial growth factor receptor tyrosine kinase inhibitor (IO/TKI). IO/TKI treatment in patients with angiogenic tumors may lead to improved clinical outcomes.

Methods

OPTIC RCC (NCT 05361720) is a prospective phase II multicenter study that assigns patients to either nivolumab/cabozantinib (angiogenic tumors, cluster 1/2) or ipilimumab/nivolumab (inflamed tumors, cluster 4/5) using a machine learning model developed from the IMmotion 151 RNAseq-based cluster definitions and the Tempus xR whole transcriptome assay. Eligibility criteria includes mccRCC without prior systemic therapy and at least one measurable lesion per RECIST 1.1. Accrual continues for patients with cluster 4/5 tumors. Patients with cluster 3/6/7 tumors were excluded. Patients assigned to cluster 1/2 are reported here. The primary endpoint is overall response rate (ORR) per RECIST 1.1 with an H_0 of 55% and H_a of 75%.

Results

76 patients were screened, 35 were assigned to the cluster 1/2 arm, and accrual is complete with 26 patients treated with nivolumab/cabozantinib. Of the 26 patients treated, cluster assignment was made from metastatic tumor for 19 patients and primary tumor for 7 patients. Patient characteristics included median age of 68 (range, 52-86), 52% male and IMDC Favorable 36%/Intermediate 56%/Poor 8%. Common metastatic sites were lung (80%), pancreas (24%), bone (16%) and liver (12%). Of the 21 patients who have received at least one post-baseline scan to date, 100% achieved a reduction in tumor burden. The RECIST best response was 71% partial response, 29% stable disease (SD), and 0% progressive disease. The tumor burden reduction in SD patients was -5%, -7%, -16%, -26%, -29%, and -29%. Three patients have progressed to date with a median follow-up 9.8 months. Nine patients (35%) experienced an SAE (any grade), including 4 thromboembolic events.

Conclusions

Using RNAseq data to assign patients with angiogenic tumors to nivolumab/cabozantinib increases ORR relative to unselected historical controls.

Clinical trial identification

NCT 05361720, accrual started 12/1/2022.

Legal entity responsible for the study

The authors.

Funding

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Disclosure

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