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Nivolumab + cabozantinib vs sunitinib in first-line treatment for advanced renal cell carcinoma: First results from the randomized phase III CheckMate 9ER trial

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Background

Results from the phase 3 CheckMate 9ER trial evaluating the checkpoint inhibitor (CPI) nivolumab (N) plus the tyrosine kinase inhibitor (TKI) cabozantinib (C) v sunitinib (S) for first-line (1L) treatment of advanced clear cell renal cell carcinoma (aRCC) are reported. As monotherapies, N and C have demonstrated efficacy and a manageable safety profile in aRCC. C has immunomodulatory properties that may counteract tumor-induced immunosuppression, providing a rationale for combining N+C.

Methods

Patients (pts) were randomized 1:1 (stratified by IMDC risk score, tumor PD-L1 expression, region) to N 240 mg flat dose IV Q2W + C 40 mg PO QD v S 50 mg PO for 4 wk (6-wk cycles) until disease progression or unacceptable toxicity (max N treatment, 2 y). Primary endpoint: progression-free survival (PFS; a $\frac{1}{4}$ 0.05 final) by blinded independent central review (BICR). Secondary endpoints (hierarchical testing): overall survival (OS; a $\frac{1}{4}$ 0.011 first interim analysis), objective response rate (ORR; a $\frac{1}{4}$ 0.05 final) by BICR, and safety.

Results

A total of 651 pts (22.6% favorable risk, 57.6% intermediate risk, 19.7% poor risk; 24.9% PD-L1 \geq 1%) were randomized to N+C (n $\frac{1}{4}$ 323) v S (n $\frac{1}{4}$ 328). With 18.1 mo median (10.6 mo minimum) study follow-up, all 3 efficacy endpoints were met. N+C significantly improved PFS (HR 0.51 [95% CI 0.41e0.64], $P < 0.0001$; median, 16.6 v 8.3 mo) and OS (HR 0.60 [98.89% CI 0.40e0.89]; $P \frac{1}{4}$ 0.0010; medians not reached) v S, and results were consistent across prespecified IMDC risk and PD-L1 subgroups. ORR (95% CI) was significantly higher with N+C v S (55.7% [50.1e61.2] v 27.1% [22.4e32.3]; $P < 0.0001$), and 8.0% v 4.6% of pts achieved complete response. Median duration of response was 20.2 v 11.5 mo for N+C v S. Any-grade TRAEs occurred in 96.6% v 93.1% of pts treated with N+C v S (60.6% v 50.9% grade \geq 3). One treatment-related death occurred with N+C v 2 with S. TRAEs led to discontinuation of S in 8.8%, N or C in 15.3%, N+C in 3.1%, N only in 5.6%, and C only in 6.6% of pts.

Conclusions

N+C demonstrated superior PFS, OS, and ORR v S in 1L aRCC. The safety profile of this combination was manageable and

consistent with the known singleagent AE profiles of N and C. These results support N+C as a new CPI+TKI option for aRCC pts.

Clinical trial identification

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