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Final analysis of the phase 3 LITESPARK-011 study: Belzutifan (bel) plus lenvatinib (len) versus cabozantinib (cabo) for advanced renal cell carcinoma (RCC) after anti-PD-(L)1 therapy

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Background

The phase 3 LITESPARK-011 study (NCT04586231) showed a statistically significant improvement in progression-free survival (PFS) and objective response rate (ORR) with bel + len vs cabo in pts with advanced ccRCC following anti-PD-(L)1 therapy at earlier analyses. Overall survival (OS) was tested but did not reach significance. We present results from the final analysis (FA) of LITESPARK-011.

Methods

Eligible adults with advanced ccRCC with disease progression after 1L or 2L anti-PD-(L)1 therapy or ≤6 mo of adjuvant anti-PD-(L)1 therapy were randomized 1:1 to receive bel 120 mg QD + len 20 mg QD or cabo 60 mg QD. PFS by blinded independent central review (BICR) per RECIST 1.1 and OS were dual primary endpoints. ORR by BICR per RECIST 1.1 was a key secondary endpoint. Duration of response (DOR) by BICR per RECIST 1.1 and safety were secondary endpoints. PFS and ORR met statistical significance at earlier interim analyses and were not formally tested at FA.

Results

A total of 747 pts were randomized (371 to bel + len and 376 to cabo). Median follow-up at data cutoff for FA (Feb 2, 2026) was 38.8 mo (range, 29.1–59.0). PFS benefit was maintained with bel + len vs cabo (median 14.8 mo vs 10.8 mo; HR 0.74, 95% CI 0.62–0.88); estimated PFS rate was 20.5% vs 12.6% at 36 mo, respectively. OS favored bel + len vs cabo with a median OS difference of 5.1 mo that was not statistically significant at FA (median 33.7 mo vs 28.6 mo; HR 0.85, 95% CI 0.70–1.03; one-sided $P=0.04689$ [prespecified boundary 0.0223]); estimated OS rate was 48.9% vs 40.6% at 36 mo, respectively. ORR was consistent with previous analyses at 53.1% with bel + len vs 40.2% with cabo. Similarly, median DOR remained longer with bel + len at 22.0 mo vs cabo at 11.9 mo. Grade ≥3 TEAEs occurred in 85.4% vs 83.0% of pts. Among pts who discontinued treatment, 173/273 (63.4%) in the bel + len group vs 203/324 (62.7%) in the cabo group received subsequent therapy.

Conclusions

At FA, PFS and ORR benefit of bel + len vs cabo was maintained. While OS favored bel + len, it did not reach statistical significance. Frequency of grade ≥3 TEAEs was similar between groups. These results continue to support the use of bel + len in advanced ccRCC following anti-PD-(L)1 therapy.

Clinical trial identification

LITESPARK-011. NCT04586231.

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Legal entity responsible for the study

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Disclosure

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