Background

- Tivozanib (TIVO) is an oral vascular endothelial growth factor tyrosine kinase inhibitor that is approved by the US Food and Drug Administration (FDA) for treatment of patients with relapsed/refractory (R/R) renal cell carcinoma (RCC) following ≥2 prior lines of therapy.

- Long-term progression-free survival (LT-PFS) is a clinically meaningful outcome for evaluating efficacy in patients with R/R metastatic renal cell carcinoma (mRCC) who received ≥2 prior lines of therapy.

- The TIVO-3 trial supported FDA approval of TIVO in R/R advanced RCC by demonstrating significantly improved efficacy outcomes over sorafenib (SOR).

- The INV PFS HR analyzed with extended follow-up (data cutoff: May 24, 2021) demonstrated significantly improved efficacy outcomes over sorafenib (SOR) for TIVO and 9.0 months (95% CI, 3.7–16.6) with SOR.

Methods

Study Design

- TIVO-3 (NCT02627964) is a phase 3, global, open-label, parallel-arm study comparing TIVO with SOR in patients with R/R advanced RCC (Figure 1).

Results

- 350 patients were randomized 1:1 to receive TIVO (n=175) or SOR (n=175). The higher LT-PFS rates with TIVO vs SOR were observed across subgroups, with clinically meaningful effects in the TIVO group (defined as ≥15% INV LT-PFS at 36 months) in patients with favorable risk status evaluated by IMDC, female sex, ECOG PS 0, age ≥65 years, and North American residence.

- Despite low numbers of patients at risk, subgroups with ≥15% INV LT-PFS at 3 years included International mRCC Database Consortium (IMDC) favorable risk, female sex, and ≥3 prior systemic regimens.

Conclusions

- INV PFS analyzed with extended follow-up was consistent with the primary IRC PS 0+1 endpoint.

- INV LT-PFS was higher with TIVO compared with SOR at every time point evaluated.

- The odds of experiencing INV PFS at 36 months with TIVO were over 5 times higher than with SOR.

A clinically relevant proportion of patients were alive and progression free at 3 and 4 years after initiating TIVO therapy compared with SOR, and this difference was consistent across all clinical and demographic subgroups evaluated.

Acknowledgments

This study was sponsored by AVEO Oncology. Editorial assistance was provided by Clara Huang, PhD, of Schoutem, Inc., a Nucleus Holding limited company, and funded by AVEO Oncology.

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