Activity of Tivozanib (AV-951) in Patients With Renal Cell Carcinoma (RCC): Subgroup Analysis From a Phase 2 Randomized Discontinuation Trial (RDT)


 OBJECTIVES

To explore the effect of RCC subtype, nephrectomy, and prior therapy on the efficacy of Tivozanib (AV-951) is a potent and selective small-molecule pan-vascular endothelial growth factor receptor (VEGFR) inhibitor with activity against the VEGFR-1, -2, and -3.

METHODS

Study Design

- Phase 2, randomized, double-blind, placebo-controlled trial
- Treatment schedule: 1.5 mg/day (open-label) for 16 weeks, followed by 12 weeks of double-blind treatment (3 cycles)

Efficacy of Tivozanib

- Objective response rate (ORR) and progression-free survival (PFS)
- Efficacy endpoints: ORR and PFS
- Efficacy was assessed in all treated patients as well as patients who attained ≥25% tumor regression

Toxicity

- Treatment-related adverse events were recorded and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.0

RESULTS

Efficacy

- ORR was higher in patients with clear cell RCC who had undergone nephrectomy (p = 0.017) and ≥25% tumor regression (p = 0.02)

- PFS was higher in patients with clear cell RCC who had undergone nephrectomy (p = 0.02)

- PFS was similar between treatment-naive and previously treated patients with clear cell RCC who had undergone nephrectomy

CONCLUSIONS

- In this exploratory retrospective analysis, the median PFS of patients with clear cell RCC who had undergone nephrectomy was 14.8 months.

- Median PFS and ORR were highest for the subgroup of patients with clear cell RCC who had undergone nephrectomy over 14.8 months.

- Median PFS was longer between treatment-naive and previously treated patients with clear cell RCC who had undergone nephrectomy.

- The adverse event profile of tivozanib was consistent with that of a selective VEGFR inhibitor with minimal "off-target" toxicities.

REFERENCES


Figure 1. Study design

Figure 2. Tivozanib PFS in all patients (ITT population; N = 272), IRR.

Figure 3. Tivozanib in patients with clear cell RCC (N = 261), IRR.

Figure 4. Tivozanib in patients with ≥25% tumor regression: 95% CI.

Figure 5. ORR and PFS analysis of patients with clear cell RCC who had undergone nephrectomy (p = 0.017, IRR).

Figure 6. Subgroup analysis of PFS by prior treatment status among patients with clear cell RCC who had undergone nephrectomy (n = 176), IRR.

Figure 7. Treatment-related adverse events observed in 10% of patients.*