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 kinases of vascular endothelial cell viability (CCV; 0.21, 0.16, and 0.2 Dm, respectively).

In a phase 1 study, the maximum tolerated dose of tivozanib was determined to be 1.5 mg/day, and responses were observed in patients with renal cell carcinomas (RCC) and other tumors.

Previously reported results from the current phase 2 study indicated that tivozanib has a safety profile similar to the maximum tolerated dose of tivozanib in phase 1 trials.

Clear cell RCC, the most common histologic subtype, has been shown to be more responsive to anti-VEGF therapies compared with non-clear cell (NCC) subtypes.

The rate of adverse events was similar across the various RCC subtypes.

In a phase 1 study, the maximum tolerated dose of tivozanib was 150 mg/day, and responses were observed in patients with clear cell RCC and other tumors.

The median duration of treatment was 8.5 months (range, 1.3-33.8 months).

The most common grade 1-2 adverse events were hypertension (clear cell, 2.2%; NCC, 2.2%) and proteinuria (4.9% and 0%).

Effect of VEGFR inhibitors has been shown to be more effective in patients with clear cell RCC compared with non-clear cell RCC.

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Effect of RCC Histologic Subtype

PFS, progression-free survival; ITT, intent-to-treat; IRR, independent radiology review; CI, confidence interval.

Effect of RCC Histologic Subtype and Nephrectomy Status

Among all treated patients, patients who had undergone nephrectomy had a significantly higher median PFS (P = 0.047) compared with those who had not undergone nephrectomy (12.6 months vs 7.1 months).

Among patients with NCC RCC, median PFS was similar between patients without (7.2 months) and with (6.6 months) nephrectomy.

Gin PFS was similar among all patient subpopulations.

Safety and Adverse Events

The most commonly reported treatment-related adverse events of any grade were hypertension (clear cell, 11.7%; NCC, 17.3%) and hypotension (clear cell, 3.5%; NCC, 6.5%) and proteinuria (4.2% and 0.5%).

The most common grade 3-4 adverse events were hypertension (clear cell, 9%; NCC, 4%) and anemia (clear cell, 2%; NCC, 2%).

In this retrospective exploratory analysis, disease control was observed for patients with all RCC histologic subtypes.

Among patients with NCC RCC, those with pulmonary (cholangio) RCC appeared to experience the greatest benefit.

The rate of adverse events was similar among patients with clear cell and NCC RCC and was consistent with that of a selective VEGFR inhibitor with minimal "off-target" toxicities.

Conclusions

- In this retrospective exploratory analysis, disease control was observed for patients with all RCC histologic subtypes.
- Among patients with NCC RCC, those with pulmonary (cholangio) RCC appeared to experience the greatest benefit.
- The rate of adverse events was similar among patients with clear cell and NCC RCC and was consistent with that of a selective VEGFR inhibitor with minimal "off-target" toxicities.

References


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Activity of Tivozanib (AV-951) in Patients With Different Histologic Subtypes of Renal Cell Carcinoma

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