Tivozanib (AV-951) is a highly potent and selective small-molecule pan-VEGFR inhibitor with activity and a favorable safety profile with single-agent tivozanib in metastatic renal cell carcinoma (RCC), colorectal cancer (CRC), and other tumor types. The objective of this Phase 1b open-label, dose-escalation trial was to determine the safety, tolerability, and MTD of tivozanib in combination with FOLFOX6 (leucovorin, 5-fluorouracil [5-FU], and oxaliplatin) in patients with advanced gastrointestinal (GI) tumors.

Four patients experienced dose-limiting toxicities during the study and discontinued tivozanib. No more than 2 prior chemotherapy regimens (≤3 lines) were allowed. A total of 22 patients have been enrolled, have received at least 1 dose of study medication, and are evaluable (≥90% of planned doses). Clinical activity was observed with FOLFOX6 or tivozanib monotherapy.

Key Eligibility Criteria

- Histologically or cytologically confirmed metastatic CRC or other GI malignancy for which FOLFOX6 is a standard treatment
- Eastern Cooperative Oncology Group (ECOG) Performance Status 0-2
- Life expectancy ≥3 months
- Adequate hematologic, liver, and renal function
- No central nervous system metastases
- No prior vascular endothelial growth factor (VEGFR) inhibitor therapy
- No current smoking
- No prior radiation therapy to the involved site
- No recent surgery (within 4 weeks)

Methods

- Sequential cohorts of 0.5, 1.0, and 1.5 mg/day oral tivozanib for 21 days followed by 7 days off
- No more than 2 prior chemotherapy regimens (≤3 lines)
- Clinical activity was observed with FOLFOX6 or tivozanib monotherapy
- No prior vascular endothelial growth factor (VEGFR) inhibitor therapy
- No current smoking
- No recent surgery (within 4 weeks)
- No prior radiation therapy to the involved site
- No recent surgery (within 4 weeks)
- No current smoking
- No prior radiation therapy to the involved site

Results from a phase 1 study determined a maximum tolerated dose of 1.5 mg/day tivozanib with FOLFOX6.
A Phase 1b Study of Escalating Doses of Vascular Endothelial Growth Factor (VEGF) Tyrosine Kinase Inhibitor Tivozanib and FOLFOX6 in Patients With Advanced Gastrointestinal (GI) Tumors

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