2544 General Poster Session (Board #2D), Mon, 8:00 AM-11:45 AM

Phase I study of c-Met inhibitor ARQ197 in combination with FOLFOX for the treatment of patients with advanced solid tumors.

Suzanne Fields Jones, Carla Kurkjian, Manish R. Patel, Jeffrey R. Infante, Howard A. Burris, F Anthony Greco, Michael Brian Hemphill, Adil I. Mohyuddin, Dana Shelton Thompson, Patrick Murphy, Eric Raefsky, Johanna C. Bendell; Sarah Cannon Research Institute, Nashville, TN; Stephenson Cancer Center/SCRI, Oklahoma City, OK; Florida Cancer Specialists/SCRI, Fort Myers, FL; Sarah Cannon Research Institute; Tennessee Oncology, Nashville, TN; Tennessee Oncology, PLLC/SCRI, Nashville, TN

Background: C-Met protein is a receptor tyrosine kinase which is overexpressed or mutated in a variety of tumor types, causing cell proliferation, metastasis, and angiogenesis. Tivantinib is an orally bioavailable small molecule which binds to the c-Met protein. This phase I study was designed to determine the maximum tolerated dose (MTD) of tivantinib in combination with standard dose FOLFOX for the treatment of patients with advanced solid tumors. **Methods:** Patients with advanced solid tumors for which FOLFOX (5-FU IV 400 mg/m^2 day 1; 5-FU CIV 2400 mg/m^2 day 1; Leucovorin IV 400 mg/m^2 day 1; Oxaliplatin IV 85 mg/m^2 day 1) would be appropriate chemotherapy received escalating doses of tivantinib BID (days 1-14) in a standard 3 + 3 design. Dose-limiting toxicities (DLTs), non-dose-limiting toxicities (NDLTs), safety, and preliminary efficacy were evaluated. **Results:** Fourteen patients (50% colorectal) were treated across 3 dose levels: 120 mg (n=3); 240 mg (n=5); 360 mg (n=6). No DLTs were observed until the 3rd dose level (treatment delay ≥3 days, secondary to grade 3 neutropenia). Common related adverse events (% grade 1/2; % grade 3/4) included: diarrhea (36%; 0%), neutropenia (0%; 29%), nausea (14%; 14%), vomiting (14%; 14%), dehydration (14%; 7%), and thrombocytopenia (14%; 0%). To date, 7 patients have been evaluated for response including 4 (57%) with stable disease evident at the 8-week evaluation (CRC, 2 patients; unknown primary favoring CRC, 1 patient; esophageal, 1 patient) and 3 (21%) with disease progression. The 4 patients with stable disease are continuing on treatment; three (CRC and unknown primary) had received prior FOLFOX. **Conclusions:** The addition of tivantinib to standard therapy FOLFOX appears tolerated up to its recommended phase II monotherapy dose of 360 mg. Preliminary efficacy is encouraging, and a phase II study is proceeding with this regimen for the first line treatment of advanced gastroesophageal patients. Clinical trial information: NCT01611857.