3508 **Oral Abstract Session, Sat, 3:00 PM-6:00 PM**

A randomized, placebo-controlled, phase I/II study of tivantinib (ARQ 197) in combination with cetuximab and irinotecan in patients (pts) with *KRAS* wild-type (WT) metastatic colorectal cancer (CRC) who had received previous front-line systemic therapy.

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Background: Tivantinib (ARQ 197) selectively inhibits the MET receptor tyrosine kinase, which is implicated in tumor cell migration, invasion, and metastasis. Resistance to EGFR inhibitors has been associated with activation of alternative pathways including MET. **Methods:** Pts with advanced *KRAS* WT CRC that progressed on or after 1 prior line of chemotherapy and no previous treatment with an EGFR inhibitor were eligible. Pts were randomized 1:1 to receive cetuximab (500 mg/m^2) and irinotecan (180 mg/m^2) on days 1 and 15 every 28 days, plus oral tivantinib (360 mg twice daily [BID]) or placebo. The primary endpoint was progression-free survival (PFS); additional endpoints include safety, objective response rate, overall survival (OS) and exploratory biomarker analyses. **Results:** Between Jul 2010 and Feb 2012, 122 pts were randomized; 117 pts were eligible for analysis (60 tivantinib, 57 placebo). Mean age was 57 years (range, 27-79 years); ECOG PS 0/1 55%/45%; and 81% received prior oxaliplatin. Median PFS was 8.3 months in the tivantinib arm vs 7.3 months in the placebo arm (hazard ratio [HR] = 0.85; 95% CI, 0.55-1.33; $P = 0.38$). Objective response rate (95% CI) was 45% (33%-58%) in the tivantinib arm and 33% (23%-46%) in the placebo arm. Median OS has not yet been reached but is trending in favor of tivantinib vs placebo (HR = 0.67). Among pts with prior oxaliplatin therapy, median PFS was 8.4 months for tivantinib and 7.2 months for placebo (HR = 0.67; 95% CI, 0.44-1.00; $P = 0.1$). The most common grade 3/4 adverse events ($\geq$ 10%) were neutropenia, diarrhea, and nausea. Correlation of clinical outcomes with additional factors including mutation status and immunohistochemical analysis of tumor MET expression will be presented. **Conclusions:** Outcomes in this trial trended towards improvement with tivantinib (360 mg BID) plus cetuximab and irinotecan, particularly in the subgroup who had previous oxaliplatin. Further studies are needed to identify the CRC population most likely to benefit from addition of tivantinib to standard therapy. Clinical trial information: NCT01075048.