

A Simon 2 stage study of 5,10 methylenetetrahydrofolic acid (CO) with 5-fluorouracil (FU) as first line treatment in metastatic colorectal cancer (mCRC).

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Background: We are conducting an open label, Simon 2 stage study to assess the safety and efficacy of CO+FU for first line treatment in mCRC. Unlike leucovorin (LV), CO directly modulates FU inhibition of thymidine synthase without the need for metabolic conversion. Preclinical models show reduced hematologic toxicity of CO+FU with enhanced efficacy compared to FU+LV. **Methods:** Eligible patients (pts), age >18 with ECOG 0-2 and measurable mCRC, w/w/o adjuvant FU+LV, irinotecan, or oxaliplatin, but no prior chemotherapy for mCRC. Pts received >2 cycles each consisting of CO 60mg/m² and FU 450mg/m² (weekly IV bolus) for 6 weeks, followed by 14 day rest. Pre-established response criteria is >4 of 23 for stage 1, >12 of 48 for stage 2. Response is defined as complete response (CR, complete disappearance), partial response (PR, >50% reduction in total tumor size), stable disease (SD, <50% reduction), progressive disease (PD, >25% increase) at week 16. **Results:** Safety data is available for 30 pts, median age 65.5 (range 42-86), F=53.3%, mean number of doses 10.2 (range 1-24). Overall incidence of grade 3/4 AEs was 2(6.6%, bowel obstruction, malignant pleural effusion). No grade 3/4 blood toxicity was observed. Response data is available for 12 pts: 3 PR, 6 SD, 3 PD. **Conclusions:** CO+FU has been well tolerated. The remaining pts are expected to be enrolled and data will be reported at the meeting.

	NCI CTCAE grade incidence (%) N=30	
	1/2	3/4
diarrhea	9 (30.0)	0 (0)
vomiting	5 (16.6)	0 (0)
neutropenia	1 (3.3)	0 (0)
thrombocytopenia	1 (3.3)	0 (0)