Introduction: The aim of this study was to determine the recommended dose of FOLFOXIRI plus cetuximab (Cmab) as first-line treatment for patients (pts) with RAS wild-type metastatic colorectal cancer.

Methods: The eligibility criteria included pts with unresectable colorectal adenocarcinoma, age 18 years or more, ECOG PS 0 or 1, wild-type or heterozygous UGT1A1*28 or *6, no history of prior chemotherapy, and adequate organ function. Patients received the combination of Cmab (initiation dose of 480 mg/m2, followed by weekly infusion of 250 mg/m2 on day 1) with FOLFOXIRI (irinotecan (CPT-11), oxaliplatin (L-OHP) 85 mg/m2, and folinate (LV) 200 mg/m2 on day 1, followed by fluorouracil (5-FU) 3200 mg/m2 infused as a 46-hour continuous infusion starting on day 1) repeated every 2 weeks. Three dose levels of CPT-11 were planned as follows: Level 1: CPT-11 165 mg/m2, Level 0 as starting dose: CPT-11 125 mg/m2, and Level -1: CPT-11 95 mg/m2. The dose-limiting toxicity (DLT) was evaluated in the first cycle. This trial was registered with the University Hospital Medical Information Network (number UMIN00001609).

Results: From May 2014 to June 2017, we enrolled a total of 8 pts (4 pts in the Level 0 and 4 pts in the Level 1). The pts characteristics were as follows: median age, 50.4 (range, 38-64); male, 3; ECOG PS 0, 6; and all left sided primary. All were assessed for safety and seven were assessed for efficacy. No treatment related death was observed. The grade 3 or 4 toxicities were neutropenia (n = 2). Among 7 pts who had at least once tumor evaluation, three (43%) were converted to the surgical resection. With a median follow-up period of 33.1 months, the time to protocol treatment failure, the median progression-free and median overall survival was 7.8 months, 8.0 months and not reached, respectively.

Conclusion: The recommended phase II dose was determined to be standard dose of Cmab with FOLFOXIRI (CPT-11 165 mg/m2, L-OHP 85 mg/m2, and LV 200 mg/m2 on day 1, followed by 5-FU 3200 mg/m2 infused as a 46-hour continuous infusion).