Methods: Patients with unresectable mCRC were randomized 1:1 to receive up to 8 cycles of FOLFOXIRI plus bev, followed by bev (arm A), or the same induction followed by bev plus metroCT (capecitabine 500 mg/tid and cyclophosphamide 50 mg/die per os, arm B) until disease progression (PD). According to the comparative Rubinstein and Korn's design, estimating a first-line PFS of 11 months, to detect a HR of 0.75 favoring arm B, with 1 sided-alpha and beta errors of 15% and 80%, 173 events were required. In the case of PD during maintenance, the re-introduction of FOLFOXIRI plus bev or of a modified FOLFOXIRI plus bev regimen (i.e. FOLFOXIRI/FOLFOX or FOLFIRI plus bev) was recommended up to 4 cycles, followed by maintenance, according to randomization arm.

Results: At a median follow up of 43.9 months, 210 and 164 progression and death events were registered. No significant differences between arms were reported in terms of PFS (median PFS arm A/B: 9.4 / 10.3 months; HR: 0.94 [70%CI: 0.82-1.09], p = 0.680) and OS (median OS arm A/B: 28 / 22.5 months; HR: 1.16 [70%CI: 0.99-1.37], p = 0.336). Response rate with FOLFOXIRI plus bev was 63% (arm A/B: 68%/57%). No interaction effect between treatment arm and RAS/BRAF status or tumour sidedness was reported in PFS or OS. In the overall study population median PFS among RAS/BRAF wt (N = 36), RAS mutant (N = 150) and BRAF mutant (N = 20) patients were 10.2, 10.1 and 9.4 months (log-rank test, p = 0.759) and median OS were 31.3, 24.9 and 19.2 months, respectively (log-rank test, p = 0.457). 152 (72%) out of 210 patients with progression event received a treatment after PD. In 87 (57%) and 44 (29%) cases FOLFOXIRI plus bev or modified FOLFOXIRI plus bev were re-introduced, respectively. Main grade 3/4 adverse events occurring during the reintroduction of FOLFOXIRI plus bev were neutropenia (20%), diarrhea (9%), stomatitis (3%), vomiting (2%), hypertension (1%), and venous thrombosis (1%).

Conclusion: The addition of metroCT to maintenance with bev does not significantly improve PFS or OS of mCRC patients irrespective of their RAS/BRAF mutational status and tumour sidedness. Activity results of FOLFOXIRI plus bev are confirmed with a shorter treatment duration (4-months). Outcome results in the BRAF mutant subgroup are consistent with previous findings with the triplet plus bev. Re-introduction of FOLFOXIRI plus bev was feasible and associated with a favourable safety profile.

O – 017 FOLFOXIRI plus bevacizumab (bev) followed by maintenance with bev alone or bev plus metronomic chemotherapy (metroCT) in mCRC: Final results of the phase II randomized MOMA trial by GONO

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Introduction: The MOMA study investigated whether the addition of metroCT to bev as maintenance treatment following 4 months of upfront therapy with FOLFOXIRI plus bev could improve PFS of mCRC patients. From May 2012 to March 2015, 232 patients, mostly RAS (65%) or BRAF (9%) mutant, were randomized in 16 Italian centers. The primary endpoint was not met. Here we provide final clinical results of the study including OS findings, subgroup analyses and treatments after progression.