respectively. Rate of patients receiving treatment after progression was similar in the two arms.

Conclusion: Although anticipating bevacizumab to chemotherapy does not improve ORR, its association with a significant longer OS suggests that the schedule of administration of bevacizumab in combination with chemotherapy could be critical to improve treatment efficacy in mCRC patients. Supported by the Italian Ministry of Health. CT.gov NCT01718873.

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P – 263 Survival analysis of a multicentre, randomized phase 3 study on the optimization of the combination of bevacizumab with FOLFOX/OXXEL in patients with metastatic colorectal cancer (mCRC)

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Introduction: Bevacizumab is a humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody, approved in combination with chemotherapy in the treatment of mCRC. It is proposed that its schedule of administration might be critical and that anticipating bevacizumab to chemotherapy might improve treatment efficacy.

Methods: mCRC patients, $\leq$ 75 years, ECOG PS $\leq$ 1 were randomized (1:1) to receive standard (S) administration of bevacizumab (5mg/kg d1 Q14) with chemotherapy (mFOLFOX/OXXEL regimen for 12 cycles) vs experimental (E) bevacizumab given 4 days before chemotherapy (same dose), at each cycle. Patients could receive maintenance bevacizumab until disease progression or unacceptable toxicity. Primary end point was the objective response rate (ORR). With 80% power and 2-tailed alpha 0.05, an expected 20% increase in response rate, 230 patients were planned. With 163 events, the study also had 80% power to detect a 0.64 hazard ratio (HR) of progression-free survival (PFS). Analyses were based on intention to treat. Correlative studies on biomarkers and FDG-PET were also planned.

Results: From May 2012 to Dec 2015, 230 patients were randomised to E (n = 115) and S (n = 115) arm. Median age was 62 (IQ range 53-68), 79% were PS 0, 93% were not pretreated, 53% had a single metastatic site, 71% had a left primary site; RAS-mutant tumors were less frequent in the S vs E arm (54/108 [47%]vs 71/108 [57%]). ORR was 54% in both arms (p = 0.89). With a median follow-up of 42 months, 209 PFS events and 150 deaths were reported. Median PFS was 10.5 and 11.7 months (HR 0.80, 95% CI: 0.61-1.06; multivariate adjusted p = 0.12) and median OS was 23.8 and 29.1 months (HR 0.70, 95% CI: 0.51-0.97; multivariate adjusted p = 0.03), in the S and E arm,