prospectively allocated to two groups according to their VEGFR2 plasma levels (ELISA-based technique, pg/ml) at study entry (VEGFR2 > 4 pg/ml favourable prognosis group, VEGFR2 ≤4 pg/ml unfavourable prognosis group). Plasma levels concentrations of other angiogenetic factors (VEGF, PlGF, HGF, VEGFR1, IL8, IL1a, T-cad, VEGFR3, SAP, VDBP, neuropilin1, CRP, endoglin) will be evaluated before the treatment start and before each cycle according to an ELISA-based technique. VEGFR2 and other angiogenic factors assessments will be centralized at the laboratory of Medical Oncology Unit – AOU Cagliari. All patients will undergo a blood test for retrieving circulating tumor DNA (Liquid Biopsy) at selected time-points before and during treatment for determining whether the status of selected tumor biomarkers evolve during tumor progression by comparing different ctDNA samples. Liquid biopsy will be performed by a central laboratory at the Unit of Cancer Genetics, ICB-CNR of Sassari. All patients will receive aflibercept in combination with FOLFIRI as for approved indication. The primary endpoint is overall survival (OS) according to VEGFR2. Secondary endpoints are Overall Survival (OS), Progression Free Survival (PFS), Response Rate, Toxicity Profile, Angiogenetic factors levels concentration before and during treatment. This study was designed to test the efficacy of aflibercept in combination with FOLFIRI (administered as for approved indication) in the second-line treatment of RAS wild type metastatic colorectal cancer patients progressing after first-line treatment with oxaliplatin, fluoropyrimidines in combination with an anti-EGFR monoclonal antibody (either panitumumab or cetuximab) and to evaluate differences in overall survival according to VEGFR2 levels. Furthermore, the DISTINCTIVE study aims to prospectively validate VEGFR2 plasma levels as predictive factor for efficacy of aflibercept in combination with FOLFIRI in the study population. The study was partially supported by Sanofi Genzyme.

P – 291 The DISTINCTIVE study: A biologically enriched phase II study of seconD-line folfiri/aflIbercept in proSpecTIvely stratified, anti-EGFR resistaNt, metastatic coloreCTal cancer patIents with RAS Validated wild typE status - Trial in progress

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Introduction: The use of chemotherapy in combination with anti-angiogenic treatment represents a standard of care in the second-line setting of metastatic colorectal cancer. In patients pretreated with an oxaliplatin-based chemotherapy either aflibercept or bevacizumab in combination with FOLFIRI are considered equivalent options. However, data regarding second-line anti-angiogenic therapy in RAS wild type patients receiving first-line anti-EGFR treatment are lacking and clinical practice is essentially based on speculations deriving from first-line studies. Moreover, biological data seem to indicate a different clinical outcome according to serum concentrations of angiogenesis-related factors, but prospective validation was not performed. VEGFR2 may play a role as predictive marker of response to antiangiogenic drugs and it should be considered a prognostic marker in patients treated with anti-VEGF therapies, as shown in both preclinical studies and exploratory analysis over randomized trials.

Methods: The DISTINCTIVE study (EudraCT-No.: 2017–002219-33; SC/2017/10687) is a biologically enriched, prospectively stratified phase II trial in RAS wild type metastatic colorectal cancer patients progressing after first-line treatment with oxaliplatin, fluoropyrimidines and an anti-EGFR monoclonal antibody. Eligible patients will be