

Session E. Gastrointestinal (colorectal) cancer

E46 Phase III study of regorafenib versus placebo as maintenance therapy in RAS wild type metastatic colorectal cancer (RAVELLO trial)

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Background: Treatment of metastatic colorectal cancer (mCRC) has improved due to the introduction of more active chemotherapies (CT) and novel targeted agents that have significantly increased response rate (RR), progression free survival (PFS) and

overall survival (OS). Recently, CORRECT and CONCUR trials have demonstrated both activity and efficacy of regorafenib, a small multi-kinase inhibitor, as monotherapy in pretreated mCRC. The wide range of action of regorafenib makes it an ideal candidate for monotherapy in earlier disease treatment lines in which different pathways could be involved in the acquisition of resistance. To improve long term efficacy of first line therapy several therapeutic approaches of maintenance treatment have been explored in mCRC

Material and methods: RAVELLO is an academic randomized, double-blind, placebo-controlled, multi-center, phase III study designed to evaluate efficacy and safety of regorafenib as maintenance treatment after first line therapy. Eligible patients: pathologically confirmed mCRC RAS wild type (KRAS and NRAS genes) treated with a first line fluoropyrimidine-based CT in combination with an anti-EGFR (epidermal growth factor receptor) monoclonal antibody for a minimum of 4 to a maximum of 8 months, with a stratification by response to the first line treatment (complete response/partial response or stable disease). 480 patients will be enrolled and randomly assigned in a 1:1 ratio to receive 160 mg regorafenib or placebo per os, every day for 3 weeks of every 4 weeks cycle, until disease progression or unacceptable toxicity. Primary endpoint is PFS. With a two-tailed alpha error of 0.05, the study will have 90% power to detect a 3-month prolongation of median PFS from randomization (corresponding to a hazard ratio of progression of 0.67 with 6-month median PFS expected in the control arm). Secondary endpoint are OS, safety, and biomarker correlative studies. Fifteen Italian centers and twentyone European centers have been involved in the trial. The First patient was enrolled on September 2014 at the Second University of Naples. Currently, 4 patients has been enrolled and are on treatment.