Phase II study of Regorafenib as single agent for the treatment of patients with metastatic colorectal cancer with any RAS or BRAF mutation and previously treated with FOLFOXIRI plus bevacizumab


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Introduction: Concomitant treatment with 5-FU, oxaliplatin and irinotecan in combination with bevacizumab (FOLFOXIRI-BEV) has demonstrated high activity and manageable toxicity and is considered as a valuable first-line option, especially for patients (pts) with RAS and/or BRAF mutated metastatic colorectal cancer (mCRC). The up-front use of this regimen raises questions about possible options for subsequent therapies. Regorafenib (REG) is an oral multikinase inhibitor that has shown benefit in overall and progression free survival (PFS) over placebo in pts with pretreated mCRC. This trial will assess safety and tolerability of regorafenib as a single agent in pts with RAS or BRAF mutant mCRC previously treated with FOLFOXIRI-BEV.

Methods: This is a multicenter phase II, single-arm, open-label study (NCT02175654). Main inclusion criteria are mCRC with any RAS or BRAF mutation; prior treatment with FOLFOXIRI-BEV regimen and progression ≤ 6 months of last dose, PS ≤ 1; evaluable disease by the RECIST criteria v1.1; adequate bone marrow, renal and hepatic function; life expectancy ≥ 90 days. Main exclusion criteria are clinically significant cardiac disease or myocardial infarction within the last 6 months, prior or concurrent presence of another neoplastic disease, and central nervous system metastases. Pts will receive regorafenib 160 mg PO, 3 weeks on/1 week off in a 4-week cycle. The primary endpoint is PFS rate at 6 months. 53 pts are needed to demonstrate that the treatment is effective if PFS rate at 6 months is higher than 30% and to reject the null hypothesis (PFS rate at 6 months ≤ 15%), considering an alpha error of 0.05 and a power of 80%. Up to date, 7 (13%) pts have been included in the study. The best treatment option for pts with RAS or BRAF mutated mCRC who have failed prior FOLFOXIRI-BEV remains an open question in the daily clinical practice. Regorafenib is an active and promising agent that could fill up this gap.