ADJUVANT REGORAFENIB IN STAGE IV COLORECTAL CANCER (CRC) AFTER CURATIVE TREATMENT OF LIVER METASTASES: A PHASE III RANDOMIZED, PLACEBO-CONTROLLED STUDY (COAST)

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Introduction: For patients with stage IV CRC and metastases confined to the liver, complete resection and pre-/peri-/post-operative chemotherapy is the standard of care. In spite of this multidisciplinary treatment approach, only a minority of patients with resected liver metastases have long-term disease-free survival. The oral multikinase inhibitor regorafenib significantly improved overall survival (OS) in patients with metastatic CRC that had progressed after approved standard therapies (CORRECT study; HR 0.77; 95% CI 0.64–0.94; one-sided p = 0.0052; Lancet 2013;381:303–312).

The current study aims to evaluate the efficacy and safety of regorafenib vs placebo in patients with CRC following curative resection of liver metastases and completion of planned chemotherapy.

Methods: This double-blind, placebo-controlled, multicenter, phase 3 study (ClinicalTrials.gov identifier NCT01939223) will randomize patients 1:1 to treatment with oral regorafenib 160 mg or matched placebo once daily in 4-week cycles of 3 weeks on, 1 week off treatment. Doses of study drug may be delayed or reduced to manage clinically significant drug-related toxicities. Treatment will continue for 2 years or until recurrence of CRC, death, intolerable toxicity, or patient/investigator decision to stop. Inclusion criteria include age ≥ 18 years, stage IV CRC, pathology-proven complete resection of liver metastases, and ECOG performance status 0 or 1. Patients must have completed adjuvant, neoadjuvant, or perioperative chemotherapy. Exclusion criteria include prior regorafenib treatment, use of strong CYP3A4 inhibitors, and completion of last treatment >8 weeks before randomization. Randomization will be stratified by number of preoperative liver metastases (<4 vs ≥4), time from diagnosis of CRC to occurrence of liver metastases (≤6 months vs >6 months), and time since last surgery for any CRC lesion (≤6 months vs >6 months). The primary endpoint is disease-free survival (DFS), assessed by the investigator using computed tomography or magnetic resonance imaging. Secondary endpoints include OS, health-related quality of life, and biomarker evaluations. Analyses will be performed when approximately 317 DFS events are observed. Enrollment of the planned 750 patients commenced in February 2014 and the estimated primary completion date is March 2018.

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