LUME-Colon 1: a Randomized, Double-Blind, Phase III Study of Nintedanib plus Best Supportive Care (BSC) versus Placebo plus BSC in Patients with Metastatic or Locally Advanced Colorectal Cancer (CRC) Refractory to Standard Therapies

Yoshino T,[1] Tabernero J,[2] Oum'Hamed Z,[3] Van Cutsem E[4]
[1]National Cancer Center Hospital East, Chiba, Japan; [2]Vall d'Hebron University Hospital, Barcelona, Spain; [3]Boehringer Ingelheim France S.A.S., Reims, France; [4]University Hospitals Leuven, Leuven, Belgium

Background: Angiogenesis is critical to CRC tumor growth and metastasis. While regorafenib has provided proof of concept for anti-VEGF therapy in patients (pts) with refractory CRC, it is associated with a specific safety profile; therefore, effective alternative treatments for refractory CRC with different safety profiles are needed. Nintedanib is a triple angiokinase inhibitor of VEGF, PDGF, and FGF signaling that is approved in the European Union (EU) for the treatment of pts with locally advanced, metastatic, or locally recurrent NSCLC of adenocarcinoma histology after first-line chemotherapy (VARGATEF®) and in the US and EU as monotherapy for the treatment of pts with idiopathic pulmonary fibrosis (Ofev®). Nintedanib has also shown signs of clinical efficacy in several other tumor types. These findings coupled with its manageable safety profile provide a rationale to investigate nintedanib in refractory CRC. The objective of this phase III study (NCT02149108; 1199.52) is to evaluate the efficacy and safety of nintedanib in combination with BSC in pts with refractory CRC after failure of standard chemotherapy and biological treatments.

Methods: Eligible pts are age ≥18 years with ECOG PS 0-1 and histologically/cytologically confirmed metastatic or locally advanced CRC adenocarcinoma not amenable to curative surgery and/or radiotherapy. Approximately 764 pts worldwide (including 20+ US sites) will be randomly assigned in a 1:1 ratio to either nintedanib (200 mg bid) + BSC or placebo (bid) + BSC in 21-day courses until disease progression, undue toxicity, or withdrawn consent. The study is powered to differentiate a clinically meaningful effect in the co-primary endpoints of PFS and OS. For both PFS and OS, the stratified log-rank test will be used to determine the effect of nintedanib independently at the two-sided 0.05 level of significance. Secondary efficacy endpoints are objective tumor response and disease control. At randomization, pts will be stratified according to previous regorafenib treatment, time from onset of metastatic disease until randomization in the trial (<24 vs ≥24 months), and region (Western Europe, North America, and Australia; Asia; and other parts of the world). Other assessments include safety measures (eg, frequency and severity of adverse events and changes in laboratory parameters), health-related quality of life, and biomarker analyses to identify potential predictive biomarkers and drug resistance mechanisms. As of May 11, 2015, 558 pts have been randomized and recruitment is ongoing. Results are anticipated in 2016.