Tumors may develop resistance to VEGF inhibitors by adopting an invasive
metastatic phenotype; the combination of Met and VEGF inhibition may result in improved clinical benefit.

**INTRODUCTION**

Met is mutated or overexpressed in a variety of human cancers, including CRC.5–8 Met activation following hypoxia has been implicated as a potentially important feedback loop between tumor cells and the vasculature.11–15 Enhanced anti-tumor activity has been observed with the combination of VEGF pathways, and the combination of Met and VEGF inhibition may result in improved clinical benefit.

**OBJECTIVES**

**Primary objective**
- To compare the PFS of patients with previously untreated mCRC receiving mFOLFOX6/bevacizumab + onartuzumab versus mFOLFOX6/bevacizumab plus placebo followed by mFOLFOX6/bevacizumab versus mFOLFOX6/bevacizumab plus placebo followed by placebo.

**Secondary objectives**
- To compare PFS with VEGF receptor-2.
- To compare PFS with C36.
- To assess for any adverse events.
- To compare survival in patients with previously untreated mCRC receiving mFOLFOX6/bevacizumab versus mFOLFOX6/bevacizumab plus placebo followed by placebo.

**STUDY DESIGN**

- **Randomized, double-blind, multicenter, placebo-controlled, two-arm, Phase II study (Figure 2).**

**STUDY POPULATION**

- Patients with previously untreated mCRC can be enrolled at a total of 10 centers. Enrolled patients will have a biopsy-proven metastatic CRC that is positive for the Met pathway.

**STUDY ENDPOINTS**

- **Primary endpoint:** Time to progression (TTP), defined as the time from randomization until objective tumor progression or death.

**SUPPORTING INFORMATION**

- **TTP:**
  - Definition: time from randomization until objective tumor progression or death.

**SUMMARY:**

- This study is open to accrual; further details can be found on ClinicalTrials.gov (NCT01119820).

**REFERENCES**