**Background**

Maintenance treatments with fluoropyrimidine alone or combined with bevacizumab after induction chemotherapy are two standard options in first-line metastatic colorectal cancer (mCRC). However, no trial has compared these two maintenance regimens.

**Inclusion criteria**

Mains inclusion criteria
- Histologically confirmed CRC;
- Measurable disease before the induction treatment;
- Unresectable metastases after induction chemotherapy;
- ECOG performance status ≤2;
- Disease control after 4-6 months of first-line chemotherapy.

Mains non-inclusion criteria
- Known brain or leptomeningeal metastases;
- Other concomitant or previous malignancy;
- Hand-foot syndrome of grade >1 during induction chemotherapy;
- Severe cardiovascular disease ≤6 months pregnancy;
- Partial or complete dihydroxyproline dehydrogenase deficiency;
- Any contraindication to bevacizumab or fluoropyrimidine.

**BEVAMANT–PRODIGE 71–FFCD 1710** is a multicenter, open-label, randomized, phase III cooperative trial of PRODIGE French intergroup (FFCD, UNICANCER GI and GERCOR networks) comparing maintenance therapy with fluoropyrimidine and bevacizumab to fluoropyrimidine alone after first-line induction chemotherapy for unresectable mCRC. The trial has started in January 2020. The theoretical end of recruitment is June 2022. The primary endpoint analysis is planned in September 2023.

**Clinicaltrials:** NCT04188145

**Randomization**

Patients are randomized after induction chemotherapy in a 1:1 ratio using the minimization technique.

**Stratification:** center, response (complete or partial response vs stabilization), performance status (0-1 vs 2), primary tumor status (resected vs no) and maintenance fluoropyrimidine (simplified USF2F regimen vs capcitabine D1 to D4 vs continuous treatment with half-dose capcitabine). The tumor evaluation performed after induction chemotherapy will be used as baseline.

**Primary endpoint:** time to treatment failure, calculated from the date of randomization (after the end of induction chemotherapy) to first radiological or clinical progression, death or end of maintenance treatment for any reason. Patients alive with no radiological progression and still under maintenance treatment will be censored at the date of last news.

**Secondary endpoints:**

- Progression-free survival (PFS1), defined as the time between randomization and the first radiological/clinical progression or death, PFS2, defined as the time between the end of maintenance treatment and radiological progression or death whatever the cause. Patients alive and without progression will be censored at the date of the last news. PFS1 and PFS2 will be calculated according to investigator’s assessment and independent centralized review.
- Overall survival;
- Toxicity according to NCI-CTC v4.0.
- Quality of life according to QLQ-C30 questionnaire.

**Statistics**

- **PFS1:** Hazard ratio (HR) and 95% confidence interval (CI) will be calculated using the Cox proportional hazard model.
- **PFS2:** Hazard ratio (HR) and 95% confidence interval (CI) will be calculated using the Cox proportional hazard model.
- **Overall survival:** will be calculated using the Kaplan-Meier method.
- **Toxicity:** will be analyzed using descriptive statistics.

**Trial objectives and endpoints**

During the maintenance treatment, patients will be evaluated for safety before each cycle. Evaluations every 9 weeks include clinical examination, biological tests, quality of life questionnaires and the same morphological exams performed at the initial evaluation. After radiological progression, patients are followed according to the local practice until death but at least every 3 months. The subsequent treatments received will be registered. The date of tumor progression after reintroduction of induction therapy or second-line therapy and the date of death will be recorded.

**Monitoring of the patients**

**Conflict of Interest T Aparicio:**

Honorary: Roche, Servier, Amgen, Breon, Sanofi, Ipsen ; Travel : Roche, Bayer

**Grant**

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