PREBICC: Prebiotic intervention in patients with advanced colorectal cancer treated with 5-FU based chemotherapy: a randomized controlled clinical intervention study

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Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON56898

Source
ToetsingOnline

Brief title
PREBICC study

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
colorectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: TKI Agri & Food (LWV20.345),Danone Global Research & Innovation Center,Nutricia

Intervention

Keyword: chemotherapy, colorectal cancer, intestinal microbiota, prebiotics

Outcome measures

Primary outcome

The main endpoints of this intervention study are the differences (*baseline vs post-intervention) in shifts of overall intestinal microbiota composition, intestinal microbiota diversity, and relative abundance of specific microbial taxa (e.g. Bifidobacterium) between the test group and control group. Based on interventions with prebiotic fibers in other populations published in the literature, and taking the variation seen in the initial analysis of our ongoing observational studies into account, we performed a preliminary power calculation. We expect to enroll a total of 62 patients with advanced colorectal cancer, 31 patients in the test group and 31 patients in the control group. This sample size is deemed necessary to ensure sufficient statistical power to observe the effects of the prebiotic fibers.

Secondary outcome

As exploratory objectives, this study will assess: (1) The feasibility, tolerance, and compliance of a nutritional intervention with a prebiotic ONS in patients with advanced CRC, (2) the effects of the prebiotic ONS on fecal and blood parameters, tumor response, chemotherapy toxicity as well as the metabolic phenotype (e.g. body weight, body composition, inflammatory profile),

and (3) the consequences for the patient-reported QoL and physical functioning

compared to a control ONS.

Study description

Background summary

Colorectal cancer (CRC) is the third most common cancer in the world. In the case of advanced CRC, the standard systemic treatment is often based on fluoropyrimidines, such as 5-fluorouracil (5-FU). 5-FU treatment has two significant drawbacks; (1) a limited proportion of patients respond to treatment, and (2) about 80% of patients experience some form of toxicity. The intestinal microbiota has been shown to modulate both and might be of influence on chemotherapy efficacy, toxicity, and quality of life (QoL). Our clinical studies and pre-clinical studies from other research groups demonstrated that intestinal bacteria and their metabolites are affected by chemotherapy and potentially influence treatment outcomes. In the context of the care for cancer patients, prebiotics are a promising strategy for intestinal microbiota modulation since they are a non-invasive and patient-friendly method to induce intestinal microbiota changes, without containing living microorganisms (in contrast to probiotics). It can therefore be concluded that targeted modulation of the intestinal microbiota with prebiotics has the potential to optimize 5-FU-based chemotherapy.

Study objective

This intervention study aims to investigate the effects of daily administration of a prebiotic fiber mixture in a Nutritionally Complete Oral Nutritional Supplement (ONS) for 8-9 weeks on intestinal microbiota composition and diversity in patients with advanced CRC treated with 5-FU-based chemotherapy compared to a control ONS. As secondary objectives, this study will assess (1) the feasibility, tolerance, safety, and compliance of a nutritional intervention with prebiotics in patients with advanced CRC, (2) the effects of the intervention on fecal and blood parameters, tumor response, chemotherapy toxicity as well as the metabolic phenotype (e.g. body weight, body composition, inflammatory profile), and (3) the consequences on the patient-reported QoL and physical functioning.

Study design

This intervention study is a double-blind randomized (1:1) controlled trial that will be performed in the Maastricht UMC+. The duration of the intervention phase for each subject will be approximately 8-9 weeks depending on the study

product intake start date, chemotherapy regime schedule, and the potential occurrence of an interruption or delay in chemotherapy.

Intervention

Patients will be stratified based on their assigned chemotherapy regimen before randomization (FOLFOX, CAPOX, and CAP). Following stratification, patients will undergo a 1:1 block randomization. Patients will be randomized to either the test group (ONS enriched with prebiotic fibers) or the control group (isocaloric, isonitrogenous ONS without prebiotic fibers). Patients will start with the prebiotic or control ONS as soon as possible, but we aim to target minimally three days before the start of the 5-FU-based treatment. Patients will take the prebiotic or control ONS two times a day during four cycles of FOLFOX or three cycles of CAPOX or CAP chemotherapy.

Study burden and risks

During the study period, patients are required to collect multiple fecal samples at their homes and complete several questionnaires. The FQ18 questionnaire, which is to be filled out only once at the beginning of the study, will take approximately 30 minutes to complete. This questionnaire is more comprehensive than the others. The other questionnaires take approximately 15 minutes to complete.
Collecting fecal samples is designed to be an easy and hygienic process that patients can manage in the comfort of their own homes. To minimize inconvenience for the patients, every research appointment will be scheduled to coincide with their regular hospital visits if possible. Furthermore, blood samples for the study will be drawn, if possible, simultaneously with the routine blood tests that are required before each treatment cycle. The test and control ONS will be provided in small bottles of 125ml to minimize the burden for the participants. To accommodate individual preferences and enhance compliance, patients will have the option to choose between two flavors: vanilla or strawberry.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

To be eligible to participate in this study, a subject must meet all of the following criteria:
- Patients diagnosed with advanced CRC who will be treated with 5-FU-based therapy (FOLFOX, CAPOX, capecitabine monotherapy)
- Simultaneous treatment with bevacizumab, panitumumab or cetuximab is allowed, provided that no systemic antibiotics are used (topical antibiotics are allowed).
- Proficient use of the Dutch language
- The patient is older than 18 years of age
- Performance (ECOG/WHO) score 0-2
- Written informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Microsatellite instability (MSI) or deficient mismatch repair (MMR) proteins
- Abnormal DPYD and/or reduced DPD enzyme function
- Presence of ileostomy
- Pregnant or nursing
- Previous systemic therapy for advanced CRC. If the patient received prior (neo)adjuvant systemic therapy, it must have been completed at least 6 months before the diagnosis of the advanced disease

- Therapeutic systemic antibiotics used less than one month before the start of the 5-FU-based treatment (topical antibiotics are allowed)
- Abdominal radiotherapy less than two weeks before the start of the 5-FU-based therapy
- Simultaneous use of other pro- and/or prebiotics during the study period (see the example list in appendix E in *E1 E2. Informatiebrief en toestemmingsformulier proefpersonen*)
- Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
- Simultaneous treatment with irinotecan-based therapy
- Known allergy to any ingredients present in the test or control ONS, requiring a fibre-free diet or suffering galactosemia or lactose intolerance
- Simultaneous participation in another medical-scientific intervention study
- Physically or mentally incapable or incompetent
- All conditions that, in the opinion of the physician, are not suitable for participation in this study (e.g. severe renal failure).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	62
Type:	Anticipated

Ethics review

Approved WMO

Date:	31-07-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL86537.068.24