Appendix 1. Supplementary materials

Supplementary table 1. Composition of the study oral nutritional supplements (ONS)

Nutritional values	Control ONS* per bottle (125ml)	Test ONS* per bottle (125 ml)
Energy	1260 kJ / 300 kcal	1256 kJ / 300 kcal
Macronutrients		
Proteins	12 g (16 en%)	12 g (16 en%)
Fat	12 g (35 en%)	13 g (39 en%)
Carbohydrates	37 g (49 en%)	32 g (42 en%)
Fibers (GOS/FOS/lvPect) **	--	4.5 g (3 en%)
Micronutrients		
Vitamins		
Vitamin A	0.30 mg	0.29 mg
Vitamin B1	0.5 mg	0.5 mg
Vitamin B2	0.5 mg	0.6 mg
Vitamin B3	2.8 mg	2.7 mg
Vitamin B5	1.7 mg	1.8 mg
Vitamin B6	0.5 mg	0.6 mg
Folic acid	80 µg	77 µg
Vitamin B12	0.9 µg	0.9 µg
Biotin	12 µg	12 µg
Vitamin C	30 mg	30 mg
Vitamin D	2.3 µg	2.3 µg
Vitamin E (α-TE)	3.8 mg	3.8 mg
Vitamin K	16 µg	16 µg
Minerals		
Sodium	120 mg	104 mg
Potassium	295 mg	286 mg
Chlorine	106 mg	103 mg
Calcium	220 mg	206 mg
Magnesium	41 mg	41 mg
Iron	4.8 mg	4.8 mg
Zinc	3.6 mg	3.6 mg
Copper	0.54 mg	0.54 mg
Manganese	1.0 mg	1.0 mg
Fluorine	0.22 mg	0.22 mg
Molybdenum	30 µg	30 µg
Selenium	17.5 µg	17.5 µg
Chromium	22 µg	20 µg
Iodine	45 µg	47 µg
Others		
Choline	110 mg	101 mg

* Both control ONS and test ONS are offered in two flavors (vanilla and strawberry) in blinded bottles

** GOS: galacto oligosaccharides, FOS: fructo oligosaccharides, lyPect: low viscosity pectin

En%: energy percentage of total

Supplementary table 2. Trial registration dataset

Data category	Information
Primary registry and trial identifying number	This study is registered in the Dutch OMON database under NL86537.068.24
Date of registration in primary registry	1 August, 2024
Source(s) of monetary or material support	TKI Agri & Food (LWV20.345) Danone Global Research & Innovation Center
Primary sponsor	Maastricht University GROW – Research Institute for Oncology and Reproduction, Maastricht University
Secondary sponsor(s)	-
Contact for public queries	
Contact for scientific queries	
Public title	PREBICC study
Scientific title	PREBICC: Prebiotic intervention in patients with advanced colorectal cancer treated with 5-FU-based chemotherapy: a randomized controlled clinical intervention study
Countries of recruitment	Netherlands
Health condition(s) or problem(s) studied	Colorectal Cancer
Intervention(s)	Active comparator: prebiotic fiber mixture ONS
	Placebo comparator: control ONS not containing prebiotic fiber mixture
Key inclusion and exclusion criteria	Ages eligible for study: ≥18 years Sexes eligible for study: both Accepts healthy volunteers: no
	Inclusion criteria: Patients diagnosed with advanced CRC who will be treated with 5-FU-based therapy (FOLFOX, CAPOX, capecitabine monotherapy) with or without simultaneous treatment with bevacizumab, panitumumab, or cetuximab, provided that no systemic antibiotics are used (topical antibiotics are allowed), proficient use of the Dutch language, and performance (ECOG/WHO) score 0-2

Data category	Information
	Exclusion criteria: microsatellite instability (MSI) and/or deficient mismatch repair (MMR) proteins, abnormal DPYD variants (single nucleotide polymorphisms) and/or reduced dihydropyrimidine dehydrogenase (DPD) enzyme function, presence of ileostomy, pregnancy or nursing, prior systemic therapy for advanced CRC (with (neo)adjuvant systemic therapy completed less than 6 months before the diagnosis of advanced disease), therapeutic systemic antibiotics used within four weeks prior to the start of 5-FU-based therapy (topical antibiotics are permitted), abdominal radiotherapy administered less than two weeks prior to the start of 5-FU-based therapy, use of pro- and/or prebiotics during the study period, inflammatory bowel disease including Crohn's disease and/or ulcerative colitis, simultaneous treatment with irinotecan chemotherapy, allergy to any ingredients in the test or control ONS requiring a fibre-free diet and/or suffering from galactosemia or lactose intolerance, participation in another medical-scientific intervention study simultaneously, physical or mental incapability or incompetence, and all conditions deemed unsuitable for study participation by the physician, such as severe renal failure.
Study type	Interventional
	Allocation: randomized intervention model. Parallel assignment masking: double blind (subject, caregiver, investigator, outcomes assessor)
	Primary purpose: prevention
Date of first enrolment	September 2024
Target sample size	62
Recruitment status	Recruiting
Main outcome(s)	The differences in shifts (∆baseline vs end of study) of the relative abundance of specific microbial taxa (e.g. *Bifidobacterium*), as well as of overall intestinal microbiota composition and diversity between test and control group.
Exploratory outcomes	Parameters assessed in feces and blood, clinical parameters, tolerance parameters and other parameters as described in the study protocol.