Aerobic fitness or Muscle mass training to Improve Colorectal cancer Outcomes (AMICO): to study safe and feasible exercise dosages (phase 2) and the effects of exercise on chemotherapy dose modifications and progression free survival (phase 3) in patients with metastatic colorectal cancer.

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Phase 2 pilot-study: to examine feasible exercise dosages in patients with mCRC and collect data on preliminary effects on clinical outcomes.Phase 3 trial: to collect data on the efficacy of exercise on 1) chemotherapy dose modifications and 2)...

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

Summary

ID

NL-OMON54043

Source
ToetsingOnline

Brief title
AMICO

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
coloncarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: NWO Vidi Grant

Intervention

Keyword: chemotherapy dose modifications, exercise intervention, feasible exercise dosages, metastatic colorectal cancer

Outcome measures

Primary outcome

Phase 2 (feasbility):

1. recruitment

2. adherence and compliance

3. participant*s and counsellors satisfaction, perceived facilitators and

barriers for implementation

4. contamination

5. adverse events

Phase 3 (effects):

1. Chemotherapy dose modifications (dose reductions, treatment delay,

discontinuation or switch)

2. Progression free survival (PFS)

Secondary outcome

Both phase 2 & 3:

1. clinical data

-treatment-related toxicity

-treatment modifications (dose reductions, treatment delay,

discontinuation, or switch) / primary outcome in phase 3 trial

-hospitalization

2. aerobic fitness

3. Immune function

4. muscle strength and mass

5. physical activity (objective and self-report)

6. physical performance (age > 70)

7. Patient reported outcomes: HRQoL, symptoms related to mCRC and its

treatment, resilience and self-efficacy.

8. Demographic and clinical covariables (tumor stage and location, ECOG,

nutritional status)

Study description

Background summary

First-line treatment of metastatic colorectal cancer (mCRC) generally includes the chemotherapies fluoropyrimidines in combination with oxaliplatin and/or irinotecan, known as doublet or triplet chemotherapy. In a previous study, we found that over 40% of patients with mCRC required dose modifications (including dose reductions, treatment delays or discontinuation) within the first three months of chemotherapy treatment, and around 30% was admitted to hospital due to chemotherapy-related toxicity. Toxicity-induced dose modifications and hospitalization may reduce benefit of treatment. In patients with mCRC, reductions in muscle mass and lower physical activity levels (<9 MET hours/week) were found to be associated with more dose-limiting toxicity and shorter (progression-free) survival. However, the causality and underlying mechanisms linking physical activity and exercise to cancer outcome have not

been elucidated. The immune system (by increased infiltration of activated NK-cells into the tumour) might play a role as was shown in studies with rodents. In addition, studies among patients showed that exercise may counteract a variety of treatment toxicities (e.g. neutropenia, neuropathy, gastrointestinal side effects, fatigue), but optimal exercise type and dose are unknown.
In addition to the above*mentioned biophysiological effects by which exercise may prevent dose modifications, several studies demonstrated the positive effects of exercise during cancer treatment on quality of life. A recent study on patients* perceptions indicated that exercise helped patients to better cope with cancer treatments, as it gave them psychological strength (i.e. empowerment and resilience) next to physical strength. We hypothesize that exercise reduces treatment-related toxicity and thereby reduces chemotherapy dose modifications and improves progression free survival (PFS). In order to conduct a sufficiently powered phase 3 randomized controlled trial (RCT) to examine the effects of exercise on chemotherapy dose modifications, it is essential to determine feasible dosages of resistance and aerobic exercise in patients with mCRC during a phase 2 trial. Studying differences in effects on chemotherapy dose modifications between different exercise programs requires a multi*arm RCT. Due to complex logistics and high costs, the conduct of a traditional adequately powered multi*arm exercise trial is difficult with available patients and resources. Therefore, we will use a Bayesian adaptive flexible multi*arm multi*stage (MAMS) design which allows for a number of interim analyses after which a treatment arm can be dropped early if it falls outside the pre*defined futility/efficacy boundaries. This reduces patients* exposure to suboptimal interventions and increases trial efficiency.

Study objective

Phase 2 pilot-study: to examine feasible exercise dosages in patients with mCRC and collect data on preliminary effects on clinical outcomes.
Phase 3 trial: to collect data on the efficacy of exercise on 1) chemotherapy dose modifications and 2) progression free survival (PFS).

Study design

Multicenter randomized controlled phase 2 and 3 trial

Intervention

Participants will be randomized into one of three study arms: 1) Continuous aerobic exercise (moderate intensity) combined with resistance exercise aiming to maintain muscle mass for 60 minutes twice a week; 2) Continuous aerobic exercise (moderate intensity) combined with high-intensity aerobic interval exercise aiming to maintain aerobic fitness for 60 minutes twice a week; and 3) a usual care control group that receives usual care. Both intervention groups

will be asked to be physically active an additional third time a week (for at least 30 min with moderate intensity) on their own according to the American College of Sports Medicine (ACSM) guidelines [26].
The intervention starts with the first cycle of chemotherapy and will continue until the end of the sixth cycle (3-week cycle) or the eight cycle (2-week cycle). After completion, 3 sessions will be offered to guide self-management to maintain exercise levels on their own. Patients from both intervention groups will be asked to stay physically active for 3 times a week and to keep doing the same sort of exercises as prescribed in the first period (T0-T2), i.e., resistance versus aerobic interval exercises. The intervention ends after 27 weeks or ends in case of disease progression or treatment switch to second line.
All groups receive a brochure with exercise guidelines based on the American College of Sports Medicine*s (ACSM) cancer-specific exercise recommendations [26].

Study burden and risks

Patients randomized to the exercise group will be guided by an physical therapist that is educated specifically on the exercise protocol for this study and are used to working with oncology patients. Therefore we expect a negligible risk for participants with regard to the exercises. Previously conducted exercise studies in advanced cancer patients appeared to be safe, with no serious adverse events reported. Patients will be screened before the physical fitness tests in the hospital on medical history which could interfere with the physical fitness tests. Therefore we expect negligible risk for participants with regard to the physical fitness tests and blood drawing. We hypothesize that the intervention is feasible. If effective, the intervention may result in less treatment-related toxicity, less chemotherapy dose modifications and increased PFS.

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

-age >=18 years;
-mCRC with indication for chemotherapy, with initially unresectable metastatic disease
-scheduled for treatment with first-line doublet or triplet chemotherapy, according to the national guideline
-able and willing to give written informed consent.

Exclusion criteria

-life expectancy <6 months
-unable to perform basic activities of daily living such as walking or biking
-presence of cognitive disorders or severe emotional instability (e.g., Schizophrenia, Alzheimer, alcohol addiction);
-presence of other disabling co-morbidities that might hamper physical exercise (e.g. heart failure (NYHA classes 3 and 4), chronic obstructive pulmonary disease (COPD, gold 3 and 4), orthopaedic conditions and neurological disorders (e.g., hernia, paresis, amputation, active rheumatoid arthritis);
-insufficient mastery of the Dutch language;
-presence of serious cardiovascular or cardiopulmonary conditions (e.g. unstable angina, arrhythmia or valve disease) such that exercise safety is at risk, as judged by the treating physician.
-Already participating in structured vigorous aerobic and/or resistance exercise >= 2 times per week comparable to our intervention

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-03-2021
Enrollment:	228
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	22-09-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-10-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-12-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	22-12-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-01-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-03-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-05-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-07-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-12-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-03-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-01-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-01-2025
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
ClinicalTrials.gov	NCT04754672
CCMO	NL72482.091.20