Oral Fecal Microbiota Transplantation Capsules from Healthy Donors in Patients with Locally Advanced, Resectable Gastric or Gastro-esophageal Junction Adenocarcinoma

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

Summary

ID

NL-OMON56807

Source
ToetsingOnline

Brief title
CAPGO

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
gastro-esophageal cancer, stomach and esophageal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Ministerie van OC&W,Cancer Center Amsterdam

Intervention

Keyword: Capsules, Chemotherapy, Gastric cancer, Microbiota

Outcome measures

Primary outcome

Primary endpoint is pathological response to chemotherapy based on the tumor regression grade. We look at the number of patients with a TRG 1-2 (complete or subtotal response) in both arms.

Secondary outcome

Efficacy and mechanism of action of fecal capsules in combination with chemotherapy for gastric and esophageal cancer.

-Pathological complete response (ypT0N0)

-R0 resection rate

-Progression-free survival and disease recurrence pattern

-Overall survival

-Incidence and severity of post-operative complications according to the Clavien - Dindo classification.

-Percentage completion of preoperative chemotherapy treatment

-Percentage withdrawal rate from surgery

-Percentage delay of surgery

-Quality of life (EORTC QLQ-C30 summary score)

-Adverse events of preoperative chemotherapy treatment

Exploratory translational and exploratory biomarker research with tumor biopsies, blood samples and fecal samples from patients. The primary purpose of this is to understand the effect of these capsules on the tumor and the immune system.

Tumor biopsies will be used to characterize the immune microenvironment by immunohistochemical stains. Biopsies can be used for DNA and RNA sequencing to investigate gene expression and mutations related to the effectiveness of the capsules. Blood samples will be used to characterize PBMCs by flow cytometry, quantify metabolites and measure cytokines. In addition, cell free DNA can be isolated from blood plasma to detect circulating tumor DNA, which can be used as a biomarker. The tumor biopsies and stool samples will also be used to quantify bacterial populations using 16S sequencing. This will allow for the microbiome to be mapped.

The stool from the fecal donors will also be examined to compare the microbiome between patients and donors.

Study description

Background summary

Despite perioperative chemotherapy and resection, gastric esophageal cancer remains a difficult condition to cure. There is increasing evidence that the microbiome influences the tumor and response to therapy. In recent research we have shown that a fecal microbiome transplant from a healthy donor prior to palliative chemotherapy can improve response. In the CAPGO study we want to investigate whether a patient-friendly microbiome intervention with fecal

capsules from allogeneic healthy donors can help chemotherapy work more effectively. These capsules have previously been tested in patients with diabetes, clostridium and colitis, where they were effective with few side effects.

Study objective

The primary goal is to demonstrate that in gastric esophageal cancer the addition of a microbiome intervention with fecal capsules from healthy donors can improve the effectiveness of perioperative chemotherapy as measured by the tumor regression grade.

Study design

This study is a randomized double-blind phase II study. Patients are divided into two groups by drawing lots. Randomization will be done between adding fecal capsules and placebo capsules. All patients receive standard perioperative chemotherapy with 4 cycles before surgery and 4 cycles after surgery. The capsules will be taken once a day for 7 days before each preoperative chemotherapy treatment. This concerns a total period of 4 weeks during which the capsules will be used.

Intervention

Fecal capsules from healthy donors. Patients should take one capsule once a day for a total of 4 weeks prior to each preoperative chemotherapy treatment for 7 days. An operation will take place after 12 weeks. After the operation, regular postoperative chemotherapy without capsules will be completed.

Study burden and risks

Taking blood samples and inserting an IV can be slightly painful and in some cases cause a hematoma.
In rare cases, gastroscopy can result in bleeding or perforation.
Patients may experience side effects from the medication and the capsules.

Side effects associated with the standard of care FLOT chemotherapy are the same as if people did not participate in the study. Include bone marrow toxicity, gastrointestinal side effects, neuropathy, hair loss and allergic reactions.

Side effects from the fecal capsules are mild and are mainly gastrointestinal such as nausea, bloating or short-term diarrhea. In addition, there is a very small chance that unknown pathogens are transferred from the allogeneic donors. The donors are extensively screened to prevent this from happening and this has

not yet occurred in other studies with these capsules.

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

Patients
-Resectable adenocarcinoma of the stomach or gastro*esophageal junction; planned start with neo-adjuvant FLOT
-Patient is fit for surgery

Healthy fecal donors
-Lean body mass of 80% or more

Exclusion criteria

Patients
Past (within 5 years) or current history of malignancy other than entry diagnosis interfering with prognosis of gastro-esophageal cancer, not including superficial and adequately treated skin and cervical malignancies.
History of a non-malignant disease of the digestive tract, such as celiac disease, chronic diarrhoea (>=3 stools/day for >4 weeks), chronic obstipation (<2 defecations/week for >3 months), Irritable Bowel Syndrome (IBS) (according to Rome IV criteria) or Inflammatory Bowel Disease (IBD).
Uncontrolled (bacterial) infections

Healthy fecal donors
-Use of antibiotics
-Infections such as HIV, hepatitis B or C
-Smoking or drug use
-Parasite infection
-Gastro-intestinal diseases such as IBS or IBD

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2024
Enrollment:	54
Type:	Anticipated

Ethics review

Approved WMO Date:	08-05-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL86412.018.24