Mapping the peritoneal immune system to identify novel immunomodulatory treatment options for diseases with peritoneal involvement.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON52795

Source
ToetsingOnline

Brief title
MAPS

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Immune disorders NEC
- Metastases

Synonym
Gastric- and colon cancer (cancer of the stomach and large intestine); peritoneal metastasis (spreading of the cancer to the abdominal wall)

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: AMC PhD Scholarship grant

Intervention

Keyword: Cancer, Immune system, Peritoneal metastasis, Peritoneum

Outcome measures

Primary outcome

The goal of this explorative study is to establish a correlation map between the healthy peritoneal immune compartment and the peritoneal immune composition in patients with peritoneal metastasized disease.

Clustering of transcriptional (scRNA-Seq) and cell surface protein expression (CyTOF) allows for identification of immune cell populations and our main study parameter will be differences in immune cell populations between peritoneal fluid from patients without peritoneal involvement and peritoneal fluid of patients with peritoneal involvement.

Secondary outcome

Not applicable

Study description

Background summary

Peritoneal metastases (PM) are observed in 10-30% of patients with gastrointestinal cancers, including colorectal and gastric cancer. The presence of PM is associated with an extremely dismal prognosis, as patients typically have limited responses to systemic therapy. In selected cases, highly invasive cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) can still be performed, but also these procedures have limited survival benefits and major comorbidity.

Because of the limited effective treatments for patients with peritoneal metastases, it is imperative to find new treatment strategies. Among the biggest breakthroughs in oncology in recent years has been the development of immunotherapy: drugs that enhance the strength of immune system to attack tumor cells. Immunotherapy has shown unprecedented durable responses even in metastasized cancers and could therefore be an exciting new therapy for patients with peritoneal metastasized cancer.
To understand how we can fully activate the immune system to fight peritoneal metastatic cancers we first have to understand the cellular and phenotypical characteristics of the peritoneal immune system in health and disease. Although it is well known that many immune cells reside in the human peritoneal cavity, the exact composition of the peritoneal immune system is unknown. Interestingly, we recently discovered that in mice, the peritoneal immune system is highly complex and consists of many subtypes of immune cells that had not yet been characterized. Peritoneal immune cells had important functions in protecting the host from excessive inflammation.
In this project, we will unravel the composition of the human peritoneal immune system and study the differences in immune composition in peritoneal metastasized cancers. This will advance our understanding on the role of the peritoneal immune system in disease, with the overarching goal of finding novel immunomodulatory treatment strategies.

Study objective

Aim
The MAPS study aims to unravel the immune composition of the human peritoneal cavity and the tumor immune environment in peritoneal metastasized gastric and colorectal cancer. The overarching aim is to find new targets for immunotherapy for this devastating disease.

Primary objectives:
To find new targets for immunotherapy for patients with peritoneal metastases, our objectives of this study are:
1) Characterization of the different immune subsets in the human peritoneal cavity
2) Identification of changes in immune subsets in patients with peritoneal metastases as compared to patients without peritoneal involvement/metastases, to identify novel immunotherapy targets.
3) Identification of changes in immune subsets in patients with inflammatory bowel disease as compared to patients without peritoneal involvement/inflammatory bowel disease to identify novel immunotherapy targets.

Study design

Longitudinal study

Study burden and risks

Since all patients are anesthetized and the abdomen needs to be entered for surgery, the additional risk of this study is negligible. The peritoneal cavity will be flushed with saline (0,9% NaCl) at body temperature. This fluid is used in standard care during surgery and is deemed safe. The only differences with standard care is that: 1) more fluid is used (approximately 1 liter of saline) to collect as many cells as possible. 2) flushing of the abdomen occurs at the start of the surgical procedure to minimize the contamination of blood immune cells. One tube of maximum 10mL peripheral blood will be taken perioperative. All patients have intravenous access during surgery, and there is no need for additional venipuncture. There is no harm expected from the additional collection of 10ml of blood, which is less than 0.2% of the patient*s blood volume. If peritoneal metastasis of the primary tumor are present, a targeted biopsy of these metastasis will be performed by the operating surgeon. If the surgical resection specimen or a part of it is considered as 'waste' material, we will sample the omentum with the milky spots for further analysis.

Benefit
There is no benefit for the patient that participates in this study. Participation in this study will hopefully lead to new insights into the composition of the human peritoneal immune system and new therapies for patients with peritoneal metastases, a disease with dismal prognosis. This will be of importance for future patients with peritoneal metastasized cancer, and potentially also for patients with peritoneal involvement in other diseases.

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

Both males and females will be included in this study. To minimize the potential risk of age and gender differences in the peritoneal immune system, we will age and gender-match the samples for analyses from the control groups and the peritoneal metastases group.
Patients are eligible when aged >18 old.

Exclusion criteria

The following general criteria will lead to exclusion from participation in this study:
a. No informed consent is provided by patient or its legal representative
b. Signs of bleeding in the peritoneal cavity, as this will lead to contamination of blood immune cells in the peritoneal cavity
c. Presence of intra-abdominal medical devices or corpus aliena, as this could elicit a local inflammatory response
d. History of active peritoneal dialysis (CAPD)
e. Recent history (<1 year) of, or active episode of peritonitis
f. History of cisplatin or oxalitplatin use. These patients will be excluded as it can hamper the analyses of samples for CyTOF.

Specific exclusion criteria per group:
Group 1: controls in which peritoneal involvement of disease is not to be suspected
a. Patients will be excluded is there are signs of inflammation such as increased CRP or leukocytosis.
b. Per-operative signs of inflammation in the peritoneal cavity such as adhesions, cholecystitis (in the cholecystectomy group).

Group 2-6: patients with cancer with/without peritoneal metastases
a. Perforation of the gastrointestinal tract

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-06-2020
Enrollment:	180
Type:	Actual

Ethics review

Approved WMO Date:	06-01-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-10-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	27-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	NL70455.018.19