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Using microscopes to observe tumor vessels

Submission date
06/10/2020

Recruitment status
No longer recruiting

Registration date
25/11/2020

Overall study status
Completed

Last Edited
13/12/2024

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
This study will investigate the tumor-associated vessels of patients with peritoneal carcinomatosis, or cancer that spreads along the inner abdominal lining. The investigators will use a technology known as intravital microscopy (IVM) in order to visualize in real-time the tumor-associated vessels of peritoneal disease. The IVM observations may determine if an individual patient's tumor vessels would be amenable to receiving systemic treatment, based on the functionality of the vessels.

Who can participate?
Patients who are undergoing surgery for peritoneal carcinomatosis

What does the study involve?
During surgery (CRS-HIPEC), a microscope will be used to directly observe the blood vessels associated with the tumor implants lining the peritoneum (abdominal lining). Intravenous (IV) dyes will be administered through catheters connected to veins in order to help enhance the microscopic observations. These dyes include a substance called fluorescein and indocyanine green, which are two generally safe and frequently used dyes for a variety of surgical procedures. Because there can be allergic reactions to fluorescein (less than 5% of cases), participants will be asked to undergo allergic skin testing to fluorescein before joining the study. This consists of a skin-prick test with a small drop of fluorescein to determine if they will have an allergic reaction. Various measurements of tumor vessels and blood flow through the vessels will be recorded.

What are the possible benefits and risks of participating?
It is not known if participation in this observational study will help or not. Possible help may include identifying tumor characteristics that may someday predict response or guide treatment in the future. Microscopic findings observed during the CRS-HIPEC may have a predictive value of PC response or recurrence. This would potentially result in improved prognostic information for you and other study participants. There is no guarantee of improved outcome for taking part in this study. Future patients may be helped from the results and information gained from this study. It is hoped that information gained in this study will aid in the understanding of cancer and help in the development of new approaches to its treatment.
It is anticipated that there will be minimal-to-no increased risk of adding a microscopic observation to the surgical procedure (CRS-HIPEC). There are, however, inherent risks to

CRSHIPEC itself. Studies have shown the complications for which patients undergoing CRS-HIPEC are at risk, including: leaking from any bowel reconnections (only in the case that bowel removal is considered part of the procedure), prolonged recovery time of bowel function (known as an ileus), and/or a decrease in blood counts (such as white blood cells, known as neutropenia) that would be temporary. However, this study is unlikely to increase these risks. Use of fluorescein may not be recommended in patients with a history of allergic hypersensitivity to fluorescein. Adverse reactions have been reported to occur in 5% or less of patients and are typically mild, including itching or hives. Adverse reactions to indocyanine green have been reported to be even lower with the incidences of mild, moderate and severe reactions to be 0.15%, 0.2% and 0.05%, respectively. Indocyanine green can cause an allergic reaction in patients who are allergic to iodine-based IV contrast dye, typically given during a CT scan. Participants who have an allergic reaction to iodine-based IV contrast dye will not be eligible to participate in this study.

Where is the study run from?
Mayo Clinic Florida (USA)

When is the study starting and how long is it expected to run for?
May 2018 to December 2024

Who is funding the study?
Mayo Clinic Florida Focused Research Teams (USA)

Who is the main contact?
Dr Emmanuel Gabriel
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Study website
https://clinicaltrials.gov/ct2/show/NCT03517852

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
NCT03517852

Secondary identifying numbers
17-009823

Study information

Scientific Title
Intravital microscopy in patients with peritoneal carcinomatosis

Acronym
IVM PC

Study objectives
This is an observational study. The purpose of this study is to evaluate the microscopic characteristics of the blood vessels associated with tumors that grow along the peritoneum. This type of study is investigational, and it is expected that the use of a special microscope will help visualize tumor-associated blood vessels and blood flow. This may lead to valuable information for physicians in the treatment of patients with this condition.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/03/2018, Mayo Clinic Institutional Review Board (Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL, USA: +1 (0)866 273 4681; IRBE@mayo.edu), ref: 17-009823

Study design
Observational single-arm pilot study

Primary study design

Observational

Secondary study design
Case series

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
https://clinicaltrials.gov/ProvidedDocs/52/NCT03517852/ICF_000.pdf

Health condition(s) or problem(s) studied
Peritoneal carcinomatosis

Interventions
During surgery (CRS-HIPEC), a microscope will be used to directly observe the blood vessels associated with the tumor implants lining the peritoneum (abdominal lining). Intravenous (IV) dyes will be administered through catheters connected to veins in order to help enhance the microscopic observations. These dyes include a substance called fluorescein and indocyanine green, which are two generally safe and frequently used dyes for a variety of surgical procedures. Because there can be allergic reactions to fluorescein (less than 5% of cases), participants will be asked to undergo allergic skin testing to fluorescein prior to enrollment in the study (as listed above). This consists of a skin-prick test with a small drop of fluorescein to determine if they will have an allergic reaction. Various measurements of tumor vessels and blood flow through the vessels will be recorded.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Identify and measure number of vessels associated with peritoneal tumor implants using intravital microscopy at the time of surgery (vessels visualized per high power field)
2. Tumor vessel density (tumor vessels per square cm area observed) as above
3. Number of tumor vessels with fluorescent dye uptake and number of tumor vessels without dye uptake)
4.Tumor blood flow (velocity, mm/sec) of the vessels and tissue penetration of fluorescent dyes as markers of vessel permeability using intravital microscopy at the time of surgery

Secondary outcome measures
1. Diameters, vessel density, detection of intravital dye and flow rates of the microvasculature of peritoneal carcinomatosis compared with normal tissue using intravital microscopy at the time of surgery
2. Pathologic features of the tumor implants (i.e. tumor grade) measured by the investigators at the time of the final pathology report (5-7 days after surgery)
3. Overall survival at 1 and 2 years

Overall study start date
08/05/2018

Completion date
31/12/2024

Eligibility

Key inclusion criteria
1. Age ≥18 years of age
2. Have an ECOG Performance Status of ≤2
3. Have measurable disease in the peritoneum by direct visualization (visible lesion typically >0.5 cm in maximal diameter)
4. Carcinomatosis that meets indications for CRS-HIPEC
5. Subject must understand the investigational nature of this study and sign an Independent Ethics Committee/Institutional Review Board approved written informed consent form prior to receiving any study related procedure
6. A negative skin-prick test to fluorescein

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
30

Total final enrolment
50

Key exclusion criteria
1. Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations
2. Renal dysfunction as defined as a GFR <45
3. Liver dysfunction as defined by Child-Pugh score >5, or LFT's 1.5x above the normal range
4. Any known allergy or prior reaction to fluorescein or ICG or a positive skin prick test to fluorescein
5. Pregnant or nursing female subjects, determined preoperatively with a urine pregnancy test
6. Unwilling or unable to follow protocol requirements
7. Any condition which in the Investigators' opinion deems the patient unsuitable (e.g. abnormal EKG)
8. Any condition that excludes CRS-HIPEC as the standard of care for the patient

Date of first enrolment
15/08/2018

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
United States of America

Study participating centre
Mayo Clinic Florida
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Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

Website
https://www.mayo.edu/research/centers-programs/cancer-research/cancer-clinical-trials/cancer-clinical-trials

Funder(s)

Funder type
Hospital/treatment centre

Funder Name

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
31/12/2020

Individual participant data (IPD) sharing plan
Current individual participant data (IPD) sharing statement as of 06/01/2022:
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository and will be available on request from the study contact.

Previous individual participant data (IPD) sharing statement:
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository.

IPD sharing plan summary
Available on request, Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		02/03/2021	06/01/2022	Yes	No