# Detection of tumor tissue in peritoneal metastases of colorectal origin using a VEGF targeted optical fluorescent imaging tracer during diagnostic laparoscopy: a single center phase 1 study

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This study has been transitioned to CTIS with ID 2024-517718-13-00 check the CTIS register for the current data. Primary Objectives:To determine the optimal dose of the VEGF-targeting optical agent Bevacizumab-IRDye800CW for an adequate tumor-...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Metastases |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON51885

**Source**
ToetsingOnline

**Brief title**
SELECT

### Condition

- Metastases

**Synonym**
Colorectal peritoneal metastases (colorectal PM)

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Groningen
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Bevacizumab-800CW, Colorectal cancer, Peritoneal metastases, VEGF-A

## Outcome measures

### Primary outcome

Degree of fluorescent signal levels (defined as TBR) per dose group, consisting

of the difference in signal levels

betweencolorectal PM and normal benign surrounding tissue.

### Secondary outcome

Correlation of the ex-vivo fluorescent signal in colorectal PM and normal

tissue with histopathology and immunohistochemistry•

Macroscopic and real-time quantification of the fluorescent signal from

pathologically confirmed colorectal PM

# Study description

### Background summary

Carefully selected patients with colorectal peritoneal metastases (PM) can be treated with curative intent by using cytoreductivesurgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC). One of the biggest challenges is to adequately selectpatients who benefit the most from this aggresive treatment, with acceptable treatment-related morbidity and mortality. Theextent of peritoneal disease, described by the peritoneal cancer index (PCI), is the most important prognostic factor for survivaland is used in the selection process. At this moment, in our clinic

white-light diagnostic laparoscopy (WL-DLS)
remains thegolden standard to diagnose and assess the extent of colorectal PM.
Unfortunately, surgeons rely on visual
inspection alone andonly clinically suspected lesions will be biopsied. Small
peritoneal tumor lesions could be easily missed and
clinically suspiciouslesions could be benign leading to underestimating or
overestimating of the extent of colorectal PM.
Therefore, there is a clearneed for a diagnostic imaging modality that can
guide the oncological surgeon in the differentiation
between tumor and benigntissue intraoperatively to get a better view of the
extent of colorectal PM.
Molecular fluorescence-guided surgery (MFGS), a promising imaging technique for
real-time intraoperative tumor detection
byusing a tumor-targeted fluorescence tracer, could serve as a *red-flag*
imaging technique to assist in optimal tumor
identification.The tracer Bevacizumab-IRDye800CW with specific affinity to VEGF
(Vascular Endothelial Growth Factor) has
been developedfor fluorescence imaging to visual tumors in the operative and
endoscopic setting. VEGF is upregulated in 93%
of colorectal PM.The results of a feasibility study with Bevacizumab-IRDye800CW
at the UMCG including seven patients with
colorectal PM werevery promising. Fluorescence signals were observed in all
patients during exploratory laparotomy. All nonfluorescent
areasproved to be benign on final histopathology. In 27 out of 57 fluorescent
areas tumor tissue was identified. If
Bevacizumab-IRDye800CW is also feasible during DLS, which is a very different
setting compared to open surgery, it might
provide a moreaccurate investigation of the extent of peritoneal disease.
Ultimately, all of these strategies may reduce
overtreatment, morbidity,and costs while maintaining the same or better
effectiveness with a lower recurrence rate and improved
quality of life

**Study objective**

This study has been transitioned to CTIS with ID 2024-517718-13-00 check the CTIS register for the current data.

Primary Objectives:
To determine the optimal dose of the VEGF-targeting optical agent
Bevacizumab-IRDye800CW for an adequate tumor-tobackground
ratio (TBR) during white-light (WL) / fluorescence-guided (FG) diagnostic
laparoscopy (WL/FG-DLS) in colorectal
PM.

Secondary Objectives:
To correlate and validate ex-vivo fluorescence signals with histopathology and

immunohistochemistry;
To quantify sensitivity and specificity of Bevacizumab-IRDye800CW for colorectal PM in order to make a power size calculationfor a possible subsequent diagnostic accuracy study

## Study design

The SELECT trial is a, non-randomized, non-blinded, prospective, single center phase I feasibility study in patients with suspicion of colorectal PM, looking at the safety profile and visibility of the VEGF-targeted tracer Bevacizumab-IRDye800CW at different doses during WL / FG-DLS. The aim is to find the dose group with the best tumor to background ratio (TBR) incolorectal PM during WL / FG-DLS. Two days prior to WL / FG-DLS, patients receive a single dose Bevacizumab-IRDye800CWintravenously. To study the safety of the tracer, hemodynamics will be monitored for up to 15 minutes after administration of the tracer. In this phase I dose-finding study, a 2x3 scheme is chosen (2 doses with 3 patients in each dose group). The single doses of Bevacizumab-IRDye800CW consist of: 4.5 mg (n = 3), 10 mg (n = 3). The first three patients receive a single dose of 4.5 mg, the following three patients receive a dose of 10 mg. After completion of the first six patients, the first interim analysis will take place to assess the safety of the tracer and determine the TBR of each dose group. The TBR is calculated using the following formula: TBR = (tumorfluorescence) / (surrounding tissue fluorescence). The dosage group with the most optimal TBR will eventually be expanded to atotal of ten patients.

## Study burden and risks

Burden: Intravenous administration of Bevacizumab-IRDye800CW two days prior to WL / FG-DLS (+/- 30 minutes)• Estimated additional operation time of 30 minutes during WL/FG-DLS.
Risks: Based on the observed toxicity profile in previous clinical trials, the risks associated with the use of Bevacizumab-IRDye800CW

Patients will have no direct benefit from this study. Surgery will be planned as usual. During surgery, no decisions will be madebased on the fluorescence imaging. The benefit of this study will be the assessment of safety and the establishment ofusefulness of Bevacizumab-IRDye800CW to identify colorectal PM during WL/FG-DLS. The results from this study will be atleast beneficial for other patients with cancer in the future.

# 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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1) Age >= 18 years;
2) Patients with colorectal PM;
3) Scheduled to undergo CRS+HIPEC in the UMCG as part of standard care for colorectal PM;
4) WHO performance score of 0-2;
5) Mentally competent person who is able and willing to comply with study procedures;
6) Signed written informed consent;
7) For female subjects who are of childbearing potential, are premenopausal with intact reproductive organs or are less than two years post-menopausal:

- A negative serum pregnancy test prior to receiving the tracer.
- Willing to ensure that she or her partner used effective birth control during the trial and for three months thereafter.

### Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1) Clinically advanced stage of colorectal PM, not suitable for CRS+HIPEC confirmed by imaging (CT/PET);
2) Has been injected with another Investigational Medicinal Product (IMP) within the past month;
3) Concomitant malignancies, except for adequately treated basocellular carcinoma of the skin or in situ
carcinoma of the cervix uteri. Subjects with prior malignancies must be disease-free for at least five years.
4) Clinically significant (i.e. active) cardiac disease (e.g. congestive heart failure, symptomatic coronary artery disease and cardiac dysrhythmia) or myocardial infarction within 12 months prior to enrolment;
5) Significant renal (creatinine>110µmol/L) dysfunction;
6) Previous allergic reaction to Bevacizumab;
7) Medical or psychiatric conditions that compromise the patient*s ability to give informed consent;
8) Pregnancy or breast feeding;
9) Any significant change in their regular subscribed or not-subscribed medication 14 days before tracer administration

## Study design

### Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 22-08-2022 |

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| Enrollment: | 13 |
| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Bevacizumab-800CW |
| Generic name: | Bevacizumab-800CW |

## Ethics review

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| Approved WMO Date: | 03-02-2022 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 11-04-2024 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |

## 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 |
|---|---|
| EU-CTR | CTIS2024-517718-13-00 |
| EU-CTR | CTIS2024-517718-13-01 |
| EudraCT | EUCTR2019-0001747-4-NL |

| Register | ID |
| --- | --- |
| CCMO | NL77451.042.21 |