Intraoperative detection of tumor tissue in peritoneal carcinomatosis of colorectal origin using a VEGF-targeted Optical Fluorescent Imaging Tracer. A single centre Pilot study (HI-LIGHT study NL45588)

Published: 09-04-2014
Last updated: 19-03-2025

Determining the feasibility and diagnostic accuracy in terms of sensitivity and specificity of intraoperative detection of peritoneal carcinomatosis of colorectal origin by intraoperative fluorescence imaging using the VEGF-targeting optical imaging...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peritoneal and retroperitoneal conditions
Study type	Interventional

Summary

ID

NL-OMON40339

Source
ToetsingOnline

Brief title
VEGF-Targeted NIR imaging in Peritoneal Carcinomatosis

Condition

- Peritoneal and retroperitoneal conditions
- Miscellaneous and site unspecified neoplasms benign
- Gastrointestinal therapeutic procedures

Synonym
colorectal, peritoneal carcinomatosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: CTMM;DFG

Intervention

Keyword: colorectal, fluorescence, peritoneal carcinomatosis, VEGF

Outcome measures

Primary outcome

- Determination of sensitivity ands specificity data of the sampled (non-) fluorescent tissue acquired intraoperatively compared to standard histopathological examination for the presence of tumor tissue. (10 samples per patient).

- Localization and (semi) quantification of a fluorescent signal of tumor tissue and surrounding tissue after post-processing of the in vivo required data.

- In vivo NIR fluorescence quantification vs. ex vivo VEGF levels in biopsies and additional ex vivo analyses (using immunohistochemistry (IHC).

Secondary outcome

Improving the detection rate of peritoneal carcinomatosa using MFR imaging, for purposes of better staging by calculating the peritoneal carcinomatosis index (PCI) based on fluorescence detection

Study description

Background summary

This project consists of the realization and clinical validation of intraoperative imaging of tumor tissue in the case of peritoneal carcinomatosis (PC) of colorectal origin. Currently, it is not possible to determine the microscopic extent of peritoneal dissemination of cancer during surgery. The decision whether or not a patient could benefit from surgery or whether the disease can be deemed as resectable or not, is based on the impression of the visual inspection of the surgeon. It seems reasonable that by resecting microscopic in addition to macroscopic disease, the number of R0 resections will increase and outcome will improve. By applying a method to assess the extent of peritoneal dissemination of cancer through a novel targeted optical fluorescent imaging methodology, both the staging and the resection will be more optimal.
VEGF-A (Vascular Endothelial Growth Factor - A) is highly upregulated in tumor tissue of patients with PC of colorectal origin (own UMCG data set: (n=35), 100%) and can be targeted by using the VEGF antibody Bevacizumab (Avastin). The objective of the proposed study is the intraoperative detection of tumor tissue of peritoneal carcinomatosis of colorectal origin by using a near-infrared fluorophore, 800CW, conjugated to bevacizumab resulting in a bevacizumab-IRDye800CW imaging compound, administered at micro dose levels (i.e. 30 nmol, or 4,5 mg). The compound has been shown to be safe at a microdosing regimen in an earlier phase I clinical study in patients with breast cancer executed at the UMCG.
Medical and surgical oncologists, pharmacists, chemists, and molecular biologists experienced in carrying out clinical translational studies using bevacizumab-IRDye800CW are involved in this project.

Study objective

Determining the feasibility and diagnostic accuracy in terms of sensitivity and specificity of intraoperative detection of peritoneal carcinomatosis of colorectal origin by intraoperative fluorescence imaging using the VEGF-targeting optical imaging agent bevacizumab-IRDye800CW in a pilot study design . Ex vivo immunohistochemical analyses and fluorescence microscopy will be used to confirm the presence of VEGF-A and bevacizumab-IRDye800CW in excised tumor tissue.

Study design

Interventional pilot study: non-randomized, open label, uncontrolled with single group assignment.
The new VEGF-targeting fluorescent tracer (bevacizumab-IRDye800CW) will be administered intravenously two days before the surgical procedure is scheduled (procedure at day 3). During the imaging procedure we will compare the tumour spots that were identified using bevacizumab-IRDye800CW with the results of the

visual inspection by the surgeon. Subsequently, the NIR fluorescent signal of different lesions will be quantified. Tumour spots will be imaged using different angles to get optimal excitation of the tissue.
Biopsies will be taken separately from areas with fluorescent and no-fluorescent spots during epi-illumination for ex vivo analyses (totalling 5 fluorescent vs 5 non-fluorescent). In addition, video registration will be performed of parts of the imaging procedure.

Intervention

Patients scheduled for a HIPEC procedure for peritoneal carcinomatosis of colorectal origin will be consented for this study. There will be three study related visits. During a screening visit (visit 1), eligibility will be evaluated and patient characteristics will be collected. During the second visit 4.5 mg of bevacizumab-IRDye800CW will be administered intravenously. The patient will then be observed for 1 hour post administration. One day after administration of the tracer (visit 3 one day before surgery) the patient is administered to the hospital as in the standard procedure. During the HIPEC procedure the fluorescent imaging will be performed and data acquired.

Study burden and risks

In this study, safety data related to (the administration of) the tracer will be collected and evaluated. Based on clinical experience in the first thirteen breast cancer patients (NL37479.042.11), animal toxicity studies and the fact that we will administrate a low, non-therapeutic (single dose 4.5 mg bevacizumab-IRDye800CW vs 5 mg/kg bevacizumab in therapeutics), no adverse events are expected following administration of bevacizumab-IRDye800CW. In the first thirteen breast cancer patients, included in NL37479.042.11, no toxicity and adverse reaction were observed. To assess more information regarding the safety of bevacizumab-IRDye800CW in the current study, safety data will be collected comparable as done in NL37479.042.11. The investigators will have close contact with the (same) investigators of NL37479.042.11 regarding safety data related to bevacizumab-IRDye800CW, collected in both studies.
In the current protocol, patients will undergo the HIPEC procedure with additional fluorescence imaging of the tumour spots found during the debulking procedure. The imaging procedure will add a maximum of 45 minutes of operation time.
The time investment of the subjects is considered reasonable. The procedures at the screening visit and the tracer administration visit will take around 4 hours total.

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.
• Patients with histopathological proven peritoneal carcinomatosis from colorectal origin who are scheduled to the HIPEC procedure
• Patient is considered to be mentally and physically fit for the HIPEC procedure as judged by the responsible physician
• WHO performance score 0-2
• Signed written informed consent.

Exclusion criteria

• 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 5 years.
• Distance metastasis (liver / lungs)

• Medical or psychiatric conditions that compromise the patient*s ability to give informed consent.
• Concurrent uncontrolled medical conditions.
• Pregnancy or breast feeding.
• Clinically significant (i.e. active) cardiac disease (e.g. congestive heart failure, symptomatic coronary artery disease and cardiac dysrhythmia, e.g. atrial fibrillation, even if controlled with medication) or myocardial infarction within the past 12 months.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-07-2014
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	image-guided surgery
Registration:	No

Ethics review

Approved WMO

Date:	09-04-2014
Application type:	First submission
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

ID: 27201
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-003066-14-NL
CCMO	NL45588.042.13
OMON	NL-OMON27201