VEGF-Targeted Near-Infrared Fluorescence imaging in Peritoneal Carcinomatosis of Colorectal Origin

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON19985

Source
NTR

Brief title
HI-LIGHT

Health condition

peritoneal carcinomatosis of colorectal cancer

Sponsors and support

Source(s) of monetary or material Support: DFG, Marie Curie, EU grant

Intervention

Outcome measures

Primary outcome

Determining the feasibility of pre-operative detection of peritoneal carcinomatosis of colorectal origin by intraoperative fluorescence imaging using the VEGF-targeting optical agent bevacizumab-IRDye800CW as confirmed by ex vivo standard histopathological and immunohistochemical analyses for the presence of tumour cells and VEGF-A expression in

excised tumor tissue en fluorescence microscopy for the bevacizumab-IRDye800CW tracer

Secondary outcome

Microscopic fluorescent signal levels observed and distribution in biopsy specimens (semi-quantitative).
Adverse events (AE), serious adverse events (SAE), and suspected unexpected serious adverse reactions (SUSARs).

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.

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 . 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. Biopsies will be extensively analysed (described below).
The intraoperative imaging procedure will be carried out at the University Medical Center Groningen, Department of Surgery.

Study population:

Ten patients scheduled for cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal carcinomatosis of colorectal cancer will undergo intraoperative near-infrared fluorescence imaging with the VEGF-targeted optical imaging agent bevacizumab-IRDye800CW .

Intervention (if applicable):

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 objective

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).

Study design

Imaging will be executed three days intravenous injection of the single dose of 4,5 mg bevacizumab-800CW during the planned HIPEC procedure

Intervention

The Clinical Trial Application presents information related to the monoclonal antibody bevacizumab labeled with the fluorescent dye IRDye800CW as injection. The injection vial contains 5.0 mg bevacizumab-IRDye800CW in 0.9% NaCl. Patients will receive a single dose bevacizumab-IRDye800CW of 4.5 mg by intravenous administration, according to the IMPD. Bevacizumab (Avastin®, Roche) is a recombinant, high affinity, humanized IgG1 monoclonal antibody with specific affinity for VEGF. The infrared dye IRDye800CW (LI-COR Biosciences, Lincoln, NE, USA) is a fluorescent dye applicable for clinical use, produced by REGIS technologies. Conjugation of the fluorescent dye to bevacizumab, purification and formulation will be performed at the department of hospital and clinical pharmacy of the UMC Groningen. The new tracer bevacizumab-IRDye 800CW has been evaluated preclinical in tumor bearing nude mice and an extended single microdose toxicity study has been performed by NOTOX, which did not show toxicity (more information can be found in the IMPD).
Patients will receive a single dose of 4.5 mg microdosing of bevacizumab-IRDye800CW, compared to a therapeutic dose of 5-10 mg/kg every two weeks. Recently, 26 renal cancer patients underwent repeated 4.5 mg 89Zr-bevacizumab administrations and imaging at baseline, 4 weeks and 6 weeks at the UMCG (NCT00831857). One patient reported nausea, redness of the face and cold extremities for 24 hours after the third tracer injection but continued bevacizumab treatment (10 mg/kg) without adverse events. No toxicity was observed in the first five breast cancer (NL37479.042.11) using bevacizumab-IRDye800CW. Based on these we do not expect toxicity of the single micro-dose administration of bevacizumab-IRDye800CW. Off course, patients will be extensively observed during the study to notify any adverse events.

Contacts

Public
University Medical Center Groningen
Department of Surgery / BioOptical Imaging Center Groningen

G.M. Dam, van
Hanzeplein 1

Groningen 9700 RB
The Netherlands
+31 (0)50 3612283
Scientific
University Medical Center Groningen
Department of Surgery / BioOptical Imaging Center Groningen

G.M. Dam, van
Hanzeplein 1

Groningen 9700 RB
The Netherlands
+31 (0)50 3612283

Eligibility criteria

Inclusion criteria

Age >=18 years, patients with histopathological proven peritoneal carcinomatosis from colorectal origin who are scheduled to undergo 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

Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2013
Enrollment:	10
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL3959
NTR-old	NTR4139
Other	: HI-LIGHT1.0
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A