A phase I/II Study to Evaluate the Safety and Feasibility of Dual-modality imaging using Indium-111-DOTA-labetuzumab-IRDye800CW in patients with Peritoneal Carcinomatosis of Colorectal Origin

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Primary objectives: To assess the feasibility, accuracy and safety of preoperative SPECT/CT and intraoperative fluorescence imaging after administration of 111In-labetuzumab-IRDye800CW in patients with PC of colorectal origin who will undergo...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Peritoneal and retroperitoneal conditions
Study type	Observational invasive

Summary

ID

NL-OMON45898

Source
ToetsingOnline

Brief title
The DuMoPEC study

Condition

- Peritoneal and retroperitoneal conditions
- Metastases
- Gastrointestinal therapeutic procedures

Synonym
Colo-rectal Peritonitis Carcinomatosa

Research involving

Human

Sponsors and support

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

Intervention

Keyword: CRS and HIPEC, Image guided surgery, Labetuzumab, Peritonitis carcinomatosa

Outcome measures

Primary outcome

To assess the feasibility, accuracy and safety of preoperative SPECT/CT and intraoperative fluorescence imaging after administration of 111In-labetuzumab-IRDye800CW in patients with PC of colorectal origin who will undergo cytoreductive surgery and HIPEC.

Secondary outcome

To assess whether additional malignant lesions can be visualised by fluorescence imaging after cytoreductive surgery, to assess the correlation between localization of the dual-labeled antibody and CEA expression in tumor and healthy tissue, and to determine the gross blood clearance of 111In-labetuzumab-IRDye800CW in patients.

Study description

Background summary

In patients with peritoneal carcinomatosis (PC) of colorectal origin and no evidence of disease outside the peritoneal cavity, survival can be improved by complete cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC). Unfortunately, conventional imaging studies cannot reliably assess the degree of intraperitoneal tumor extension. Therefore,

patient selection for HIPEC can only be done accurately by abdominal inspection during surgery. Up to 13% of patients are considered inoperable during surgery . Due to the presence of adhesions and scar tissue in the peritoneal cavity of these patients (often as result of previous surgery), tumor deposits may be difficult to detect with the naked eye and/or palpation. Sensitive preoperative imaging may help to select patients eligible for CRS and HIPEC. Once selected for surgery patients* prognosis depends on the completeness of cytoreductive surgery, which may be improved using intraoperative imaging. The dual-labeled anti-CEA antibody labetuzumab, 111In-labetuzumab-IRDye800CW, enables both preoperative SPECT/CT imaging to assess the intraperitoneal tumor load preoperatively, as well as intraoperative fluorescence imaging to detect and visualize tiny tumor deposits during surgery. Labetuzumab is a humanized monoclonal antibody specifically directed against carcinoembryonic antigen (CEACAM5), which is overexpressed in approximately 95% of colorectal cancers (CRC). Four or five days after administration of this tracer a SPECT/CT scan can be acquired to determine the intraperitoneal cancer extension. Subsequently, the fluorescent (IRDye800CW) signal can be used during cytoreductive surgery to detect and visualize tumor nodules.

Study objective

Primary objectives: To assess the feasibility, accuracy and safety of preoperative SPECT/CT and intraoperative fluorescence imaging after administration of 111In-labetuzumab-IRDye800CW in patients with PC of colorectal origin who will undergo cytoreductive surgery and HIPEC.

Secondary objectives: To assess whether additional malignant lesions can be visualised by fluorescence imaging after cytoreductive surgery , to assess the correlation between localization of the dual-labeled antibody and CEA expression in tumor and healthy tissue, and to determine the gross blood clearance of 111In-labetuzumab-IRDye800CW in patients.

Study design

This is a single centre, open label, single arm intervention study. Patients will receive a single intravenous dose of 111In-labetuzumab-IRDye800CW (100 MBq). A protein dose escalation study will be performed to assess the optimal dose of the dual-labeled antibody for intra-operative dual-modality imaging. The first 15 patients will receive a single intravenous dose of 2, 10 or 50 mg of 111In-labetuzumab-IRDye800CW. Five patients per dose level will be included. After assessment of the optimal dose, the 14 following patients will receive the lowest dose that still has optimal fluorescence imaging characteristics.
At day 4 or 5 after antibody injection a SPECT/CT scan will be acquired and the peritoneal carcinomatosis index (PCI) will be scored by two independent observers.

One or two days after the SPECT/CT scan patients will undergo standard surgical resection of intraperitoneal tumors extended with the use of fluorescence imaging and image-guided surgery. After completion of the surgical resection, the peritoneal cavity will be examined for residual tumor tissue by fluorescence imaging and additional suspected tumor lesions may be removed after critical appreciation of the surgeon on malignant aspect. Subsequently the patient will undergo a standard of care HIPEC procedure. After surgery, the surgical specimens will be analyzed microscopically, immunohistochemically (CEA expression) and by gamma counting to quantitatively determine the uptake of the radiolabeled antibody. Adverse events will be monitored and and estimation of blood clearance of the tracer will be determined by taking blood samples at different time (moments of least possible patient burden) points after injection.

Study burden and risks

The risks associated with the antibody injection are negligible. Radiolabeled labetuzumab preparations have been administrated to more than 100 patients at doses up to 100 mg per patient without significant or clinically relevant toxicity, except for mild allergic reactions. Toxicity tests in rats and mice have been performed with IRDye800CW and IRDye800CW-conjugated antibodies and no adverse reactions were seen. In non-human primates a small increase of QTc-interval was seen after administration of cetuximab-IRDye800CW. This was considered to be a cetuximab-mediated effect and no QTc-prolongation has been observed in clinical trials with IRDye800CW-conjugated girentuximab or bevacizumab (currently more than 70 patients at the Radboud UMC and UMC Groningen).
Patients will undergo a thoraco-abdominal body SPECT/CT scan and three 3 ml blood samples will be taken to monitor safety (blood chemistry, liver and kidney function) and to determine the intravenous dose. Effective radiation dose of a 100 MBq 111In*labeled IgG: labetuzumab-IRDye800CW will be 22 mSv, the total dose calculated for the surgeon is 180 µSv per year (index yeardose 0.18). Considering the patient category (metastatic CRC) this is considered an acceptable dose according to the ICRP 62. On the day of surgery fluorescence imaging will be used intraoperatively. This will not be an extra risk or burden to the patient. Image-guided surgery using tumor-targeting dual-label antibodies could significantly and clinically relevantly improve oncological surgery, justifying this study.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein zuid 10
Nijmegen 6525GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein zuid 10
Nijmegen 6525GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Clinical diagnosis of peritoneal carcinomatosis of colorectal origin.
Scheduled for cytoreductive surgery and HIPEC.
Age over 18 years
Signed informed consent

Exclusion criteria

Any medical condition present that in the opinion of the investigator will affect patients* clinical status.
Administration of a radionuclide within 10 physical half- lives prior to study enrollment
Pregnancy or lactation
Very high (>500 ng/ml) serum CEA levels
Immunohistochemically proven non-CEA expressing primary tumor (if analyzed in primary tumor resection specimen)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-10-2018
Enrollment:	29
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	111-indium-DOTA-labetuzumab-IRDye800CW
Generic name:	111-indium-DOTA-labetuzumab-IRDye800CW

Ethics review

Approved WMO Date:	13-06-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-12-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	11-12-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2016-001882-99-NL
CCMO	NL57505.091.16