Validation of Uptake of a VEGF-targeted Optical Fluorescent Imaging Tracer in Surgical Specimens of Breast Cancer and Application of Pre- and Intra-operative Human Molecular Fluorescence Imaging Techniques. A multicenter feasibility study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON39185

Source
ToetsingOnline

Brief title
VEGF-Targeted Fluorescent Tracer Imaging in Breast Cancer

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: breast cancer, optical imaging, VEGF

Outcome measures

Primary outcome

Patient related study procedures

The study consists of a total of five study procedure related visits. During a screening visit, eligibility will be evaluated and patient characteristics will be collected. During the administration visit (3 days before surgery), pre-operative optical imaging will take place and a blood sample will be taken. Subsequently, 4.5 mg of bevacizumab-IRDye 800CW will be administered intravenously. The patient will then be observed for 4 hours. Thereafter, another optical imaging procedure will take place and a blood sample will be taken. During a visit approximately 36 hours after administration of the tracer, an optical imaging procedure will take place. Directly before surgery, an optical imaging procedure will take place and a blood sample will be taken. During surgery, the MFRI camera will be used to detect a fluorescent signal. At an outpatient visit (approximately 10 days after surgery), the last blood sample will be taken.

Study aims

- (Semi-)quantification and localization of a fluorescent signal of tumor,

tumor margins, surrounding tissue and lymph nodes in surgical specimens.

- Collection of safety data of Bevacizumab-IRDye800CW and to assess

immunogenicity.

- Localization of Bevacizumab-IRDye 800CW in (sub-)cellular compartments.

- (Semi-)quantification and localization of a fluorescent signal of tumor,

tumor margins, surrounding tissue and lymph nodes prior and during surgery by

MFRI.

- Exploration of optimal imaging time point, pharmacokinetics and localization

of a fluorescent signal of tumor, surrounding tissue and lymph nodes

pre-operative.

- Correlation of collected data to VEGF levels and other (VEGF related)

biological parameters.

Secondary outcome

n.a.

Study description

Background summary

To improve breast cancer management, there is a need for better visualization of presence and extent of breast cancer. Molecular imaging of breast cancer associated targets is a promising technique to accommodate this need. Vascular Endothelial Growth Factor (VEGF), which is differentially expressed in normal versus (pre)malignant breast tissue, has proven to be a valid target for molecular imaging. Fluorescent labeling of bevacizumab (a VEGF targeting humanized monoclonal antibody currently used in therapy) has potential advantages over radioactive labeling in view of radiation safety, infrastructure, costs and stability. Therefore, the fluorescent tracer bevacizumab-IRDye 800CW has been developed and was recently approved to be

administered to patients in a tracer dose. To detect this tracer in vivo, intra-operative Multispectral Fluorescence Reflectance Imaging (MFRI) cameras are available at both institutions. Advanced optical imaging systems are operational at both centers for pre-operative imaging. These systems can be evaluated in clinical studies with this new fluorescent tracer.

Study objective

The primary objectives of this study are (1) to assess uptake of bevacizumab-IRDye 800CW in breast cancer, surrounding tissue and lymph nodes as measured in surgical specimens after a single intravenous administration of 4.5 mg and (2) to evaluate safety aspects of the tracer.
Secondary objectives are to assess the ability of pre- and intra-operative optical fluorescence imaging systems to detect a fluorescent signal from bevacizumab-IRDye 800CW in vivo and explore their potential utility.

Study design

In this non randomized, non blinded, prospective, multicenter feasibility study, the new VEGF-targeting fluorescent tracer (bevacizumab-IRDye800CW) will be administered to patients with proven breast cancer. In both centers, a part of the surgical specimen will be investigated extensively to determine uptake of bevacizumab-IRDye800CW in tumor and surrounding tissue (localization, (semi-) quantification). Also, the MFRI camera will be used in both centers during the surgical procedure to visualize a fluorescent signal of the tumor, surrounding tissue and lymph nodes (localization, semi-quantification). In both centers, optical imaging modalities will be used to image patients at several time points after administration and before surgery to visualize, localize and semi-quantify a fluorescent signal in tumor tissue, tumor margins, healthy tissue and lymph nodes to explore pharmacokinetics and optimal imaging time points.

Intervention

All included patients receive an injection with fluorescently labeled bevacizumab (5mg) once.
Blood samples will be taken at 4 time points. The first and second time, 4mL blood will be drawn. The 3rd time, 12 mL will be drawn. The 4th time 8 mL will be drawn.

Study burden and risks

In this study, safety data related to (the administration of) the tracer will be collected and evaluated. Based on pre-clinical experiments, toxicity studies and the low administered dose, no adverse events are expected. Given the first application of this tracer in man all safety precautions will be taken into

account. To do so, the first 3 patients will be treated with a time interval of two weeks and the first 5 patients will be treated in one center only (UMC Groningen). Also, immunogenicity will be determined in blood samples.
The risks related to the blood withdrawal are considered minimal, only 12 ml of blood is withdrawn (in comparison, 500ml of blood is withdrawn during a blood donation), divided over four visits.
The risks related to the use of the MFRI camera are considered minimal. A small increase in surgical procedure time is expected. Trained personnel to work with the camera are available in the operating room. Risks related to the use of the pre-operative imaging systems are considered minimal, as the systems are approved to be used in clinical research studies.
The time investment of the subjects is considered reasonable. The procedures at the screening visit will take about 1 hour, at the tracer administration visit about 6 hours, at the tracer uptake visit about 1 hour and before surgery about 1 hour.

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 proven breast cancer (cytology, histology) who are scheduled to receive operation intervention.
Tumor size of at least 5 mm (0,5 cm) diameter according to anatomical imaging data.
Signed written informed consent.
Able to comply with the protocol.
WHO performance score 0-2.

Exclusion criteria

- Other invasive malignancy.
- Serious other medical conditions.
- Pregnant or lactating women. (Documentation of a negative pregnancy test must be available for pre-menopausal women with intact reproductive organs and for women less than two years after menopause).
- Prior radiotherapy on the involved area.
- Major surgery within 28 days before the initiation of the study.
- Prior allergic reaction to immunoglobulins or immunoglobulin allergy.
- Prior neo-adjuvant chemotherapy.
- Breast prosthesis in target breast.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-03-2012

Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	07-09-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-12-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-06-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-12-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-05-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-08-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-10-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-01-2014
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-04-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-09-2014
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
EudraCT	EUCTR2011-003083-75-NL
CCMO	NL37479.042.11

Study results

Date completed:	16-07-2014
Actual enrolment:	20