Determine the feasibility of detecting endometriosis during surgery using a molecular targeted fluorescent imaging tracer

Published: 22-06-2016
Last updated: 16-04-2024

The main objective of this pilot study is to investigate the feasibility of fluorescence imaging with the fluorescence agent bevacizumab-800CW to detect endometriosis tissue.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms female benign
Study type	Interventional

Summary

ID

NL-OMON46122

Source
ToetsingOnline

Brief title
Detection of endometriosis using optical molecular imaging

Condition

- Reproductive neoplasms female benign
- Obstetric and gynaecological therapeutic procedures

Synonym
Endometriosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Researchgrant Optical Molecular Imaging Group

Intervention

Keyword: Endo-Light

Outcome measures

Primary outcome

The aim of this feasibility study is to investigate whether the fluorescent agent bevacizumab-800CW can specifically target endometriosis lesions as determined by ex vivo fluorescence imaging techniques. This will be confirmed by standard H/E staining, VEGF immunohistochemistry, confocal laser endomicroscopy (CLE), spectroscopy and histopathological fluorescence microscopy. In this way, future intra-operative quantification and visualisation of endometriosis can be evaluated.

Secondary outcome

The secondary objective of this study is to investigate whether the Olympus NIRlaparoscope is able to detect endometriosis lesions intraoperatively by fluorescence imaging after micro dosing injection of 4,5 mg bevacizumab-800CW.

Study description

Background summary

The aim of this pilot project is to determine the feasibility of fluorescence imaging to improve the treatment of endometriosis in the future. Incomplete resection of endometriosis lesions often results in recurrence of symptoms and the need for repeated surgery, with considerable associated morbidity. The value of the fluorescence imaging with the near infrared (NIR) fluorescent agent bevacizumab-800CW will be evaluated in vivo and ex vivo to determine the feasibility in specific detection of endometriosis lesions in patients that are

undergoing surgery for endometriosis. Secondly, there will be a clinical validation of intra-operative fluorescence imaging in the laparoscopic treatment of endometriosis using a CE-certified Olympus NIR laparoscope. This intra-operative imaging technique can be used as a tool to detect more lesions, resulting in a more radical resection and lower risk of recurrence of symptoms compared to current standard laparoscopy. In a previous immunohistochemicaltissue study, VEGF-A was shown to be significantly over-expressed inendometriosis tissue compared to surrounding normal healthy tissue, justifying the use of the VEGF-A-targeted bevacizumab-800CW.In a recent clinical trial in patient with breast cancer, colorectal cancer, and oesophageal cancerbevacizumab-800CW appeared to be safe and specific for VEGF-A(NCT01508572,NCT01972373, NCT02129933, NCT02113202 at www.clinicaltrials.gov).

Study objective

The main objective of this pilot study is to investigate the feasibility of fluorescence imaging with the fluorescence agent bevacizumab-800CW to detect endometriosis tissue.

Study design

Interventional feasibility study: non-randomized, open label, uncontrolled with single group assignment. Patients planned to undergo laparoscopic surgery for endometriosis will be consented for this study. Three days before surgery, patients receive an intravenous injection of 4,5 mg bevacizumab-800CW. During surgery, white light and fluorescence images will be taken. All clinical suspected endometriosis lesions are removed by gold standard white light imaging. To be able to correlate the absence or presence of fluorescent signals with endometriosis, surgeons will biopsy non-suspicous lesions when fluorescent (up to 5) and when non-fluorescent (up to 5). Directly after surgery the surgeon indicates the suspicious and unsuspected lesions at the surgical specimen. The surgical specimen will be scanned in the BlackBox fluorescence imaging system to evaluate presence of fluorescence in these lesions. Ex vivo correlation between fluorescent signals in endometriosis specimen by fluorescence flatbed scanning haematoxylin/eosin and VEGF immunohistochemistry will performed using ex vivo imaging techniques. These procedures are all carried out at the University Medical Centre Groningen, in a collaboration between the Department of Surgery, Nuclear Medicine and Molecular Imaging and Intensive Care, the Department of Gynaecology and the Department of Pathology.

Intervention

Three days before surgery, the patient receives an intravenous injection of 4,5 mg bevacizumab-800CW. During laparoscopy, white light and fluorescence images are taken with the Olympus NIR camera system and all endometriosis tissue is

taken out by gold standard white light imaging. Up to 5 fluorescent and up to 5 non-fluorescent biopsies are taken of non-suspicious lesions. White light fluorescence images are taken ex vivo of the surgical specimen, to confirm if the tracer accumulates specifically in endometriosis tissue. Biopsies of fluorescent and non-fluorescent peritoneal surface tissue will be taken only if technical feasible and safe for reasons of comparison.

Study burden and risks

The burden associated with participation consists of an intravenous injection of 4,5 mg bevacizumab-800CW threedays before the surgical procedure, requiring admission to the hospital for one to one and a half hour. Additionally, the surgical procedure will be slightly
longer, due to the use of the intraoperative fluorescence imaging (no more than 30 minutes).

1. The possible serious adverse event for injection of bevacizumab-800CW is an allergic and anaphylactic reaction, as described in the IMPD of METc application 2011/196, but has not been observed in more than 100 patients currently injected with the tracer. Potential other adverse events are transient and mild (nausea, vomiting, flushing, chest discomfort), but have not been observed in now more than 100 patients injected with the tracer.
2. The possible effect of prolonged anaesthesia because of testing the camera system and detection of residual disease is limited in itself because of a total extra surgery time of no longer than 30 minutes.
3. There is no risk or burden of using the intraoperative imaging device; all mandatory tests have been executed and tested to be safe for use in patients and the camera system is confirmed with a CE marking.
4. There is no risk of infection; the imaging device is sterilized according to standard procedures at the Central Sterilisation Unit at the UMCG to prevent infection during surgery.
5. If the surgeon considers it safe, biopsies are taken from clinical non-suspicious lesions when fluorescent (up to 5) and non-fluorescent surrounding tissue (also up to 5). The risk of complications due to these biopsies is considered as low.

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

1. Females aged * 18 years
2. Scheduled for surgery for the treatment of endometriosis
3. WHO performance score of 0-2
4. Written informed consent
For female subjects who are of childbearing potential, are premenopausal with intact reproductive organs or are less than 2 years post-menopausal:
4. A negative serum pregnancy test prior to receiving the second generation tracer
5. Willing to ensure that she or her partner uses effective contraception during the trial and for 6 months thereafter.

Exclusion criteria

1. Medical or psychiatric conditions that compromise the patient*s ability to give informed consent ;2. Pregnancy
3. History of infusion reactions to Bevacizumab or other monoclonal antibody therapies
4. Significant renal, cardiac, or pulmonary disease (ASA III-IV)

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):	28-04-2017
Enrollment:	10
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	22-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-07-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	26-07-2017
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	EUCTR2016-001362-28-NL
ClinicalTrials.gov	NCT02975219
CCMO	NL57269.042.16

Study results

Date completed:	31-05-2018
Actual enrolment:	4

Summary results
Trial is onging in other countries