Intraoperative near-infrared fluorescence imaging of endometriosis with OTL38: a pilot study

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Primary objective:- To assess the feasibility of a single intravenous injection of OTL38 in detecting endometriosis during surgery by determining the concordance between fluorescent signal and histopathological confirmed endometriotic tissue.- To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Obstetric and gynaecological therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON48378

Source
ToetsingOnline

Brief title
OTL38 in endometriosis

Condition

- Obstetric and gynaecological therapeutic procedures

Synonym
Endometriosis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: OnTarget Laboratories

Intervention

Keyword: Endometriosis, Fluorescence guided surgery, OTL38

Outcome measures

Primary outcome

Primary endpoint:

- To determine the sensitivity or true positive rate (TPR) for OTL38 in combination with NIR fluorescence imaging, defined as the proportion of fluorescent positive tissue samples (of resected tissue or biopsies) that are histologically confirmed endometriotic tissue and FR+ relative to the total number of tissue samples confirmed to be FR+ and endometriotic tissue. Sensitivity = (True Positive)/(True Positive +False Negative).

- False positive rate (FPR) for OTL38 in combination with fluorescent light, for the purpose of this protocol, will be calculated as 1 * the Positive Predictive Value (PPV) and is defined as the proportion of fluorescent positive tissue samples removed (of resected tissue or biopsies) that are histologically confirmed to be non-endometriotic tissue by the pathologist relative to the total number of tissue samples removed with fluorescent light imaging. False Positive Rate = (False Positives) / (True Positives + False Positives).

- Incidence rates of all treatment-emergent AEs (TEAEs), adverse device effects (ADEs), and SAEs, from the time of OTL38 administration until follow-up visit 3.

Secondary outcome

Secondary endpoint:

- The proportion of lesions identification with OTL-38 and NIR that could not

otherwise be identified by white light and finger palpation.

Study description

Background summary

Endometriosis is affecting millions of reproductive-aged women worldwide and is associated with substantial morbidity, including pelvic pain, multiple operations, and infertility. The mainstay of diagnosis has been visualisation of lesions by laparoscopy or laparotomy. Surgery is also the preferred method of treatment for severe endometriosis aiming for removal of as many lesions as possible. The diagnosis of peritoneal endometriosis may be difficult due to the polymorphic aspects of the lesions. Enhanced intraoperative detection of endometriosis lesions with fluorescence imaging has the potential to provide better identification and radical resection of peritoneal endometriosis.
Folate receptor * (FR*) is expressed on endometriotic tissue and OTL0038, a folate analog ligand conjugated to an indole cyanine like green dye developed as an imaging agent for patients with tumors or benign tissue that overexpress FR*, could be suitable for targeted intraoperative imaging of endometriosis.

Study objective

Primary objective:
- To assess the feasibility of a single intravenous injection of OTL38 in detecting endometriosis during surgery by determining the concordance between fluorescent signal and histopathological confirmed endometriotic tissue.
- To assess the safety and tolerability of single intravenous dose of OTL38.

Secondary objective:
- Localization of occult endometriotic lesions with NIR imaging and OTL38, that would otherwise remain invisible with white light only.

Study design

* This is a phase 2, single-center, single dose, open-label pilot study in endometriosis patients scheduled to undergo surgery.
* Each patient will be dosed with 0.025 mg/kg OTL38 intravenously.

Intervention

* Infusion of OTL38 0.025 mg/kg.

Study burden and risks

Risks:
Hypersensitivity reactions
Risks of taking blood samples: pain, bruising, infection
Presence of a camera system in the operating room

Burden:
Extra time investment
The risks of participation for the subjects in the trial include hypersensitivity reactions. These risks are deemed minimal. Nevertheless precautionary measures (supervised administration by qualified staff and availability of medical treatment to treat hypersensitivity reactions) are in place and these effects are generally well manageable. The burden of the trial is minimal, the research will for the largest part coincide with routine care and the proposed procedures are minimally invasive. We therefore believe this research that, could possibly provide a useful tool to increase detection of endometriosis spots.

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. Female (premenopausal) patients 18 years of age and older
2. Patients scheduled for elective surgery (laparoscopic or laparotomy) for the diagnosis or treatment of endometriosis
3. WHO performance score of 0-2
4. A negative serum pregnancy test at screening followed by a negative serum pregnancy test on the day of surgery or day of admission for female patients of childbearing potential
5. Female patients of childbearing potential agree to use an acceptable form of contraception from the time of signing informed consent until 90 days after study completion
6. Ability to understand the requirements of the study, provide written informed consent and authorization of use and disclosure of protected health information, and agree to abide by the study restrictions

Exclusion criteria

1. Previous exposure to OTL38
2. Any medical condition that in the opinion of the investigators could potentially jeopardize the safety of the patient
3. History of anaphylactic reactions
4. History of allergy to any of the components of OTL38, including folic acid
5. Pregnancy (or positive pregnancy test) or breast-feeding
6. Presence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule
7. Impaired renal function defined as eGFR< 50 mL/min/1.73m2
8. Impaired liver function defined as values > 3x the upper limit of normal (ULN) for alanine aminotransferase (ALT) or aspartate aminotransferase (AST), alkaline phosphatase (ALP), or total bilirubin
9. Received an investigational agent in another investigational drug or vaccine trial within 30 days prior to surgery
10. Known sensitivity to fluorescent light

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-07-2019
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	OTL38
Generic name:	OTL38

Ethics review

Approved WMO

Date:	31-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	06-02-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	08-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2018-003693-27-NL
CCMO	NL67992.056.18
Other	Trial NL7607