A Single Ascending Dose, Open Label, Exploratory Study of OTL-038 for the Intra-operative Imaging of Folate Receptor Alpha Positive Ovarian, Renal Cell and Endometrial Cancer

Published: 23-06-2014
Last updated: 21-04-2024

Primary Objectives1. To assess the safety and tolerability of ascending doses of a single IV injection of OTL-0382. To assess the efficacy of ascending doses of a single IV injection of OTL-038 in detecting ovarian, renal cell and endometrial cancer...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON42083

Source
ToetsingOnline

Brief title
Study for Intra-operative Imaging of Cancer using OTL-038

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
.renal cell and endometrial carcinoma / ovarian, primary ovarian, renal and endometrial cancer

Research involving

Human

Sponsors and support

Primary sponsor: On Target Laboratories, LLC
Source(s) of monetary or material Support: Sponsor;On Target Laboratories LLC

Intervention

Keyword: cancer, fluorescent probe, image guided surgery

Outcome measures

Primary outcome

Efficacy endpoints

1. TBR, defined as fluorescent signal of tumor tissue compared to fluorescence signal of tissue surrounding the tumor, at different doses;

2. Concordance between the pathology results with respect to the presence of cancer and the imaging assessment;

3. Number and location of FR-a+, cancer+ tumor lesions or resection margins identified under usual visual/tactile conditions, under both usual visual/tactile conditions and fluorescent light, and under fluorescent light only

4. Surgeons* opinion regarding utility of IV OTL-038 injection and imaging system

Tolerability / safety endpoints

Treatment-emergent adverse events (TEAEs) using MedDRA from the time of administration throughout the study period, and changes in serum biochemistry, hematology, urinalysis, vital signs, ECG, injection site status, and physical

examination findings.

Pharmacokinetic endpoints

Cmax, T*, AUC, Tmax, Clearance, urinary excretion

Secondary outcome

n/a

Study description

Background summary

It is important to improve visualization of tumors and metastases, such as in ovarian, renal cell and endometrial cancer, in real time during surgery to enable the surgeon to excise more of the tumor, and also to facilitate proper staging. Intra-operative identification of cancer tissue using new real-time imaging modalities that could provide clear tumor identification and demarcation would provide a very useful tool to reduce positive resection margins and increase full removal of the tumor hence reducing rates of re-interventions and therefore may reduce morbidity and improve patient outcome. Furthermore, if otherwise invisible tumor lesions and metastasis can be identified, tumor staging will be possibly improved which influences treatment choices. In the last few years, a novel optical imaging platform has emerged. The use of fluorescent probes that recognize cancer-specific antigens, in conjunction with a clinical imaging system, are under investigation.
OTL-038, a fluorescent probe that targets FR-a, a receptor over-expressed in most ovarian, renal cell and high risk endometrial cancers, and that emits lights with wavelengths in the near-infrared (NIR) spectrum, along with an imaging system, can be used to visualize folate receptor alpha (FR-a) positive cancer in patients during surgery. This could enable the surgeon to excise more of the tumor tissue as compared to usual visual and tactile methods.

Study objective

Primary Objectives
1. To assess the safety and tolerability of ascending doses of a single IV injection of OTL-038
2. To assess the efficacy of ascending doses of a single IV injection of OTL-038 in detecting ovarian, renal cell and endometrial cancer during surgery by :

a. Tumor to background ratio (TBR)
b. Concordance between fluorescent signal and tumor status of resected tissue
c. Detection of more FR-a+, cancer+ tumor lesions and resection margins with fluorescent light compared to usual visual/tactile conditions
3. To assess the surgeons* opinion regarding the utility of OTL-038 IV injection and imaging system in cancer surgery
4. To assess the pharmacokinetics of ascending doses of a single IV injection of OTL-038

Exploratory Objectives
1. To assess the efficacy of different imaging systems ex-vivo by
a. Back table TBR

Study design

Phase 2, open-label, exploratory study

Study burden and risks

Risks
Hypersensitivity reactions
Risks of taking blood sample: pain, bruising, infection
Presence of a camera 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 reduce positive resection margins hence reducing rates of re-interventions and increase the identification rate of otherwise occult malignant lesions and possibly improves patient outcome and may be used in staging procedures, is justified.

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

Inclusion criteria ovarian cancer:
1. Known or high clinical suspicion of primary ovarian cancer planned for either primary debulking surgery or interval debulking surgery by laparotomy (18 patients)
2. Clinical suspicion of primary ovarian cancer planned for either laparoscopic staging procedure or laparoscopic procedure to determine optimal primary treatment (debulking surgery procedure vs neo-adjuvant chemotherapy) (15 patients);Inclusion criteria renal cell cancer:
1. Known or high clinical suspicion of primary renal cell carcinoma planned for either primary radical nephrectomy by laparotomy or laparoscopy (3 patients) or partial nephrectomy by laparoscopy (15 patients)
Inclusion criteria endometrial cancer:
1. Known or high clinical suspicion of primary endometrial carcinoma planned for either primary staging or debulking surgery by laparotomy or laparoscopy (15 patients)
Inclusion criteria general:
1. 18 years of age and older
2. Normal or clinically acceptable medical history, physical examination (including vital signs), and laboratory tests at screening

3. Patients are clinically fit for surgery

Exclusion criteria

1. Any condition that in the opinion of the investigators could potentially jeopardize the health status of the patient
2. History of anaphylactic reactions or severe allergies
3. History of allergy to any of the components of OTL-038, including folic acid
4. Pregnancy, or positive pregnancy test
5. Clinically significant abnormalities in ECG and/or clinical laboratory test results
6. Presence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial
7. Impaired renal function defined as eGFR<50 ml/min/1.73m2
8. Impaired liver function defined as values greater than 3x the upper limit of normal (ULN) for ALT, AST, or total bilirubin.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-09-2014
Enrollment:	66
Type:	Actual

Medical products/devices used

Generic name:	Artemis Handheld Camera System
Registration:	Yes - CE intended use

Product type:	Medicine
Brand name:	OTL-038
Generic name:	n/a

Ethics review

Approved WMO Date:	23-06-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-08-2014
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-03-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	13-08-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	31-08-2015
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2014-002352-12-NL
CCMO	NL49686.058.14