An open-label, mass balance study to investigate the absorption, distribution, metabolism and excretion of [14C]-OTL0038 after a single intravenous dose to healthy volunteers.

Published: 30-07-2019
Last updated: 10-04-2024

Primary objectives:To determine the mass balance of drug-related radioactivity following i.v. administration of a single dose of [14C]-OTL0038 in humans.To determine the primary route and mechanism of excretion of drug-related radioactivity...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48212

Source
ToetsingOnline

Brief title
CS0326 On Target

Condition

- Other condition

Synonym
ovarian cancer

Health condition

imaging agent for overian cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: absorption, distribution, excretion, metabolism

Outcome measures

Primary outcome

Radioactivity and Pharmacokinetic Parameters

Total radioactivity and PK parameters will be derived by non-compartmental analysis from total radioactivity-time as well as unchanged parent drug-time profiles.

Safety and Tolerability Parameters

Baseline is defined as the last available and evaluable value measured prior to [14C]-OTL0038 administration (vital signs, ECG, laboratory parameters), unless otherwise specified.

The following are defined as safety/tolerability parameters:

Adverse events

Vital signs

12-lead ECG

Clinical laboratory parameters

Local tolerability

Weight

Physical examination

Calculation of Mass Balance

Individual plasma and whole blood total radioactivity as well as unchanged parent drug (LC-MS/MS) data will be used to directly obtain Cmax and tmax, respectively.

Mass balance will be calculated as the percent of total administered radioactivity recovered in urine and feces. To calculate mass balance, the amount of administered radioactivity is defined as the total radioactivity in the dosing solution minus any radioactivity loss due to adsorption to the infusion bag, etc.

The PK parameters on total radioactivity as well as unchanged parent drug (LC-MS/MS) data in plasma and whole blood will be based on actual blood sampling times [h] (relative to the corresponding administration time) rounded to two digits and negative pre-dose times will be set to zero.

Secondary outcome

Vital signs values;

Clinical laboratory values;

Number of subjects with adverse events (AEs);

12-lead ECG values.

Local tolerance

Weight

Physical examination outcomes.

Study description

Background summary

On Target Laboratories has developed OTL38, a folate analog conjugated with an indole cyanine green dye as a tumor-specific imaging agent. OTL38 binds specifically to the high affinity FR and functions as an imaging agent in patients with tumors that overexpress FRα. Following i.v. infusion of OTL38, the agent distributes throughout the body and is rapidly cleared from the circulation, while areas with a high concentration of folate receptors, such as several carcinomas, retain the agent. When OTL38 is excited by light between the wavelengths of 760-776 nm (maximum excitation at 774-776 nm), it emits light (fluoresces) at wavelengths in the near-infrared (NIR) spectrum (maximum emission 794-796 nm). This fluorescence of the malignant tissue is captured by an imaging system that can be used by the surgeon, along with normal perioperative procedures such as palpation and visual observation, to decide which tissues to remove during cytoreduction surgery.
OTL38 is currently in clinical stage development for both ovarian cancer (phase 3) and lung cancer (phase 2). A complete overview of all pre-clinical and clinical studies conducted with OTL38 can be found in the Investigator*s Brochure.

Study objective

Primary objectives:
To determine the mass balance of drug-related radioactivity following i.v. administration of a single dose of [14C]-OTL0038 in humans.
To determine the primary route and mechanism of excretion of drug-related radioactivity following intravenous administration of a single dose of [14C]-OTL0038 in humans.
To estimate the plasma exposure of metabolite(s) as a percentage of total drug-related exposure.
Profiling of [14C]-OTL0038 metabolites in blood, urine and feces.

Secondary objective:
To evaluate the safety and tolerability of [14C]-OTL0038 after a single intravenous dose.

Study design

The present study is designed to investigate the absorption, metabolism, and excretion of OTL0038 as well as the safety/tolerability of OTL0038 following the administration of a single i.v. dose to healthy subjects.

Intervention

Up to 8 healthy male subjects will receive a single 60 minute i.v. infusion of 1.75 mg [14C]-OTL0038 containing approximately 105 µCi radioactivity.

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the IMPD for further information.

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. Able to provide informed consent to participate in this study after reading the participant information sheet and informed consent form and after having

the opportunity to discuss the study with the Investigator or designee.
2. Healthy and free from clinically significant illness or disease as determined by medical history, physical examination, laboratory and other tests at Screening.
3. Male Caucasian subjects, aged 18 to 60 years (inclusive) at Screening.

Exclusion criteria

1. Any finding of the medical examination (including blood pressure, pulse rate and ECG) deviating from normal and of clinical relevance.
2. History or current clinically significant gastrointestinal, hepatic, renal, respiratory, cardiovascular, metabolic, immunologic, hormonal disorders.
3. History of any major surgery within the last 4 weeks before Screening or any bone fracture within the last 2 months before Screening.

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):	04-12-2019
Enrollment:	8
Type:	Actual

Ethics review

Approved WMO

Date:	30-07-2019
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-10-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-01-2020
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	EUCTR2019-002985-10-NL
CCMO	NL70868.056.19

Study results

Results posted: 11-01-2021

First publication
16-11-2020