A Phase 1 Trial to Assess the Mass Balance, Absolute Bioavailability, and Pharmacokinetics of 14C ASTX660 in Healthy Volunteers

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON49455

Source
ToetsingOnline

Brief title
Mass Balance and Pharmacokinetics of 14C-ASTX660 in Healthy Volunteers

Condition

- Other condition
- Leukaemias

Synonym
advanced solid tumors, lymphoma

Health condition

solid tumors, lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Astex Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: 14C-ASTX660, Bioavailability, Mass balance, Pharmacokinetics

Outcome measures

Primary outcome

To identify and quantify the main excretion pathways of ASTX660, including the mass balance of excretion in urine and feces.

Secondary outcome

To determine the oral absolute bioavailability (F) of ASTX660 after single dose administration in the fasted condition.

To determine the fraction of ASTX660 dose absorbed (Fa).

To determine the PK of ASTX660 following oral and IV administration.

To determine the safety and tolerability of ASTX660 following oral and IV administration.

To identify the metabolites of ASTX660 in plasma, urine, and feces, if feasible.

Study description

Background summary

ASTX660 is a new compound that may eventually be used for the treatment of patients with advanced solid tumors, lymphoma, and acute myeloid leukemia and

for whom standard life-prolonging measures are not available.

ASTX660 is in development and is not registered as a drug but has been given to humans before.

Study objective

The purpose of this study is to investigate how safe the new compound ASTX660 is and how well it is tolerated when it is administered to healthy volunteers. ASTX660 has been administered to humans before. It has also been previously tested in the laboratory and on animals.

It will also be investigated how quickly and to what extent ASTX660 is absorbed and eliminated from the body. ASTX660 will be labeled with 14 Carbon (14C) and is thus radioactive. In this way ASTX660 can be traced in blood, urine and feces. The additional radiation you will be exposed to in this study is negligible.

Study design

The actual study will consist of 2 periods: the volunteer will stay in the research center for 6 days (5 nights) (Period 1) and up to 11 days (10 nights) (Period 2), with at least 4 days between the end of Period 1 and the start of Period 2.

ASTX660 will be given as an oral capsule with 240 milliliters (mL) of tap water and an intravenous infusion (solution of the compound that will be administered directly in a blood vessel). On Day 1 in Period 1, 1 hour after receiving ASTX660 as an oral capsule, the colunteer will receive 100 microgram (µg) containing 14C-radiolabeled ASTX660 as an intravenous injection. On Day 1 in Period 2, the volunteer will receive 120 mg ASTX660 containing 14C radiolabeled ASTX660 as a single oral capsule.

During the first 4 hours after oral administration of the study compound the volunteer is not be allowed to lie down (except when told you can by responsible doctor or study staff), as this may influence the uptake of the study compound.

The planned treatment for the study is as follows:

Day Study
Compounds
Formulation How often
Day 1, Period 1 ASTX660, 120
mg Oral
capsule Once

Day 1, Period 1 ASTX660, 100 µg containing 14C radiolabeled ASTX660 Intravenous solution, injection Once
Day 1, Period 2 ASTX660, 120 mg containing 14C radiolabeled ASTX660 Oral capsule Once

Intervention

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Study burden and risks

The study compound may cause side effects.

ASTX660 has been administered to 152 patients with advanced solid tumors and lymphomas. The following side effects were most frequently observed (in >=15% of patients or more) in these patients:
• fatigue
• increased lipase level in the blood
• increased amylase level in the blood
• nausea
• diarrhea
• vomiting
• anemia
• skin rash / skin rash with spots and bumps
• constipation
• pruritus (itching)
• increased alanine aminotransferase level in the blood
• edema peripheral (fluid retention)
• cough

The study compound may also have side effects that are still unknown.

Possible discomforts due to procedures
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

In total, we will take about 360 mL of blood from you. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time.

To make a heart tracing, electrodes will be pasted at specific locations on your arms, chest and legs. Prolonged use of these electrodes can cause skin irritation.

Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the volunteer to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

Exposure to radiation
This study involves using radioactive markers. The additional radiation burden in this study due to the administration of radiolabeled ASTX660 is study is negligible.

If you participate in scientific research involving exposure to radiation more often, you should discuss with the responsible doctor whether participation would be safe.

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

Gender: Male or female
Age: 18 to 65 years, inclusive, at screening
Body mass index: 18.0 to 30.0 kg/m2, inclusive at screening

Exclusion criteria

1. Employee of PRA or the Sponsor.
2. History of significant drug and/or food allergies.
3. Using alcohol in the 48 hours (2 days) prior to screening and each admission to the clinical research center is not allowed.
4. Using tobacco products in the 3 months prior to screening.
5. Known significant mental illness or other condition, such as active alcohol, or other substance abuse or addiction, that in the opinion of the Investigator predisposes the subject to high risk of noncompliance with the protocol.
6. Positive drug and alcohol screen (opiates, methadone, cocaine, amphetamines [including ecstasy], cannabinoids, barbiturates, benzodiazepines, tricyclic antidepressants, and alcohol) at screening and each admission to the clinical research center.

See the protocol for the complete overview

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-09-2020
Enrollment:	8
Type:	Actual

Ethics review

Approved WMO Date:	21-04-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-09-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-10-2020
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	EUCTR2020-000193-26-NL
CCMO	NL73633.056.20

Study results

Date completed: 06-11-2020

Results posted: 21-07-2022

First publication
07-06-2022