A Phase 1 Study to Assess the Mass Balance, Absolute Bioavailability, and Pharmacokinetics of 14C-ASTX029 in Healthy Volunteers

Published: 12-09-2022
Last updated: 07-04-2024

Primary objectives:To identify and quantify the excretion pathways of oral ASTX029, including the mass balance and the excretions in urine and feces (Period 1).To determine the absolute oral bioavailability (F) of ASTX029 under fasting conditions (...

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

Summary

ID

NL-OMON51576

Source
ToetsingOnline

Brief title
CS0387-220219

Condition

- Other condition

Synonym
solid tumors

Health condition

advanced solid tumors

Research involving

Human

Sponsors and support

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

Intervention

Keyword: bioavailability, mass balance, pharmacokinetics

Outcome measures

Primary outcome

• The amount of radioactivity excreted in urine and feces with an objective to

recover >=90% of the radiolabeled ASTX026.

Secondary outcome

• Concentration-time profile and PK parameters of total radioactivity from

analysis of plasma, urine, and feces collected at identified timepoints.

• PK parameter estimates for ASTX026 in plasma.

• [14C]-metabolic profile and identified metabolites in plasma blood.

• Major radioactive peak/metabolites in the urine and fecal radiochromatograms

as a percentage of the radioactive dose.

• Incidence and severity of treatment emergent adverse events (TEAEs).

Study description

Background summary

ASTX029 is a synthetic small molecule that acts as an inhibitor of the extracellular signal-regulated kinases (ERK) 1/2, which are serine/threonine kinases that comprise a key component of the mitogen-activated protein kinase (MAPK) signaling pathway.
ERK activity is commonly upregulated in cancer, as a result of activating

mutations within upstream components of the MAPK pathway, such as rat sarcoma virus (RAS) and Rapidly accelerated fibrosarcoma (RAF).
ASTX029 has been evaluated comprehensively in preclinical toxicology studies and has not shown unacceptable toxicities. ASTX029 was also negative in genotoxicity panel including Ames assay, chromosomal aberration and in vivo micronucleus assay. For more details on the pre-clinical and clinical studies conducted with ASTX029, please see the Investigator*s Brochure.

Study objective

Primary objectives:
To identify and quantify the excretion pathways of oral ASTX029, including the mass balance and the excretions in urine and feces (Period 1).
To determine the absolute oral bioavailability (F) of ASTX029 under fasting conditions (Period 2).

Secondary objectives:
To determine the fraction of an ASTX029 oral dose absorbed (Fa).
To determine the plasma and urine pharmacokinetics (PK) of ASTX029 following oral and intravenous (IV) administration of 14C-ASTX029.
To determine the safety and tolerability of ASTX029 following the sequential oral and IV administrations of non-radiolabeled and 14C-ASTX029, respectively.
To identify and quantify the metabolites of ASTX029, if feasible.

Study design

Phase 1 open-label, 2-treatment period fixed-sequence study of single doses of ASTX029 in healthy subjects.

Intervention

IMP and formulations: 14C-ASTX029 solution, 14C-ASTX029 IV formulation and ASTX029 tablet
Route of Administration: Oral (tablet and solution) and intravenously (IV) (solution) administration

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the overall benefit risk in the CSP 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. Male subjects and female subjects of non-childbearing potential , aged 18 years to 65 years, inclusive, at Screening.
2. Body mass index (BMI) of 18.0 kg/m2 to 32.0 kg/m2, inclusive, and at Screening.
3. Women of non-childbearing potential should be surgically sterilized or physiologically incapable of becoming pregnant or should be postmenopausal. Surgically sterile women are defined as those who have had a hysterectomy, bilateral ovariectomy, or bilateral tubal ligation. Women who are surgically sterile must provide documentation of the procedure. Postmenopausal women must have had >=12 months of spontaneous amenorrhea (with documented follicle-stimulating hormone (FSH) >=33.4 mIU/mL). All women must have a negative pregnancy test result at Screening and on Day -1 of Period 1.

4. Male subjects, if not surgically sterilized, must agree to use adequate contraception and not donate sperm from first admission to the clinical research center until 90 days after the follow-up visit. Adequate contraception for male subjects who are sexually active with women of childbearing potential (WOCBP) entails the use of a latex or other synthetic condom during any sexual activity with WOCBP until 90 days after the follow-up visit. Total abstinence, in accordance with the lifestyle of the subject, is also acceptable.
5. Satisfactory physical and mental health at Screening and on Day -1 on the basis of medical history, physical examination, clinical laboratory, 12-lead electrocardiogram (ECG) in triplicate, and vital signs, as judged by the Principal Investigator.

Exclusion criteria

1. Employee of clinical research organization (CRO) or the Sponsor.
2. Clinically significant systemic allergic disease or a history of significant drug and/or food allergies, including, but not limited to, a history of anaphylactic reactions, or allergic reactions due to any drug and/or food leading to significant morbidity.
3. Use of any prescription drugs within 30 days or 5 half-lives (whichever is longer) prior to each admission to the clinic.
4. Use of any non-prescription drugs (excluding paracetamol), vitamin preparations and other food supplements, or herbal medications (eg, St John*s Wort) within 14 days prior to each admission to the clinic.

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):	10-01-2023
Enrollment:	8

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap.
Generic name:	Nap.

Ethics review

Approved WMO Date:	12-09-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-02-2023
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	EUCTR2022-002656-39-NL
CCMO	NL82249.056.22