A randomized, placebo-controlled, double-blind, single ascending dose study to evaluate the safety, tolerability and pharmacokinetics of NX210 in healthy volunteers.

Published: 16-04-2020
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Primary objective:To assess the safety and tolerability of single doses of i.v. administered NX210.Secondary objective:To assess the PK of NX210 via its metabolite NX210c in plasma after single doses of i.v. administered NX210.Exploratory objectives...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Spinal cord and nerve root disorders
Study type	Interventional

Summary

ID

NL-OMON49076

Source
ToetsingOnline

Brief title
CS0332-190166 Axoltis

Condition

- Spinal cord and nerve root disorders

Synonym
Neurological disorders; spinal cord injury

Research involving
Human

Sponsors and support

Primary sponsor: Axoltis Pharma
Source(s) of monetary or material Support: Axoltis

Intervention

Keyword: pharmacodynamics, pharmacokinetics, safety, tolerability

Outcome measures

Primary outcome

The following are defined as safety/tolerability parameters:

Physical examination;

(Serious) adverse events (SAEs and AEs);

Clinical laboratory assessments including hematology, biochemistry and

urinalysis;

12-lead ECG;

Telemetry;

Vital signs;

Local tolerability.

The following are defined as PK plasma parameters for NX210 via its metabolite

NX210c (calculated using a non-compartmental model):

Maximum concentration (Cmax);

Time to Cmax (tmax);

Terminal elimination rate constant (Kel);

Terminal elimination half-life (t1/2);

Area under the concentration-time curve (AUC) from time of dosing (zero) to

time t of the last measured concentration above the limit of quantification

(AUC0-t);

AUC under the concentration-time curve from time zero to infinity (AUC0-inf);

Total clearance (CL);

Volume of distribution (Vz).

Secondary outcome

Nap

Study description

Background summary

NX210 is a chemically synthesized peptide of 12 natural amino acids derived from SubCommissural Organ (SCO)-spondin. SCO-spondin is a large multi-domain glycoprotein of 4.500 amino acids, specific to the Central Nervous System (CNS) extracellular matrix (ECM) and secreted by specialized ependymocytes located in the SCO, a highly conserved structure located in the roof of the third brain ventricle of all vertebrates [1].
NX210 targets to diseases belonging to CNS dysfunctions, like traumatic spinal cord injury (SCI), or memory loss/cognitive disorders.

NX210 preclinical data demonstrated efficacy in 2 animal models of SCI and cognitive impairment in IP route, which can be transposed to the intravenous (i.v.) route in human.

Although NX210 precise mechanism of action is still under investigation, preclinical data showed that NX210 has properties usually looked for human treatment of any neurological disorder, i.e. neuroprotection, neuroregeneration, remodeling and cellular plasticity mechanisms induction, or reduction in inflammation, mainly in intraperitoneal (IP) route.

Study objective

Primary objective:
To assess the safety and tolerability of single doses of i.v. administered NX210.

Secondary objective:

To assess the PK of NX210 via its metabolite NX210c in plasma after single doses of i.v. administered NX210.

Exploratory objectives:
To assess the PD of NX210 by analyzing biomarkers and exploring the neurophysiological effects of NX210 on electroencephalography (EEG) after single doses of i.v. administered NX210.
To assess the PK/PD relationship of NX210 after single doses of i.v. administered NX210.
To assess potential anti-drug antibodies after single doses of i.v. administered NX210.

Study design

Single site, randomized, placebo-controlled, double-blind, single ascending dose study in healthy male and female subjects.

Intervention

Five (5) single ascending doses of NX210 are planned to be tested in 5 cohorts of 8 healthy subjects each. In each cohort, subjects will be randomized in a 3:1 fashion to NX210 or placebo.

Study burden and risks

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

Subject is a male or is a female of non-childbearing potential, aged between 18 and 55 years (inclusive).
A body weight of >=50.0 kg and <=90.0 kg (85.0 kg for Cohort 5 at the highest dose) and a body mass index (BMI) of >=18.0 kg/m2 and <=30.0 kg/m2 at Screening.
Healthy as determined by the Investigator, based upon a medical evaluation including medical history, physical examination, neurological examination, lab tests and ECG performed at screening.
Subjects understand the study, can give written informed consent at Screening, and are willing to comply with the requirements and restrictions of the study.

Exclusion criteria

Prior or ongoing medical condition, medical history, physical findings, ECG findings, laboratory or vital signs abnormality that, in the Investigator's opinion, could adversely affect the safety of the subject.
The subject has a current or recurrent disease (e.g., cardiovascular,renal, liver, gastrointestinal, malignancy or other conditions) that could affect the distribution, metabolism or excretion of the investigational product or could affect clinical or laboratory assessments.
History of any clinically significant allergy, hypersensitivity or intolerance.
Subject with one or more of the following laboratory abnormalities at Screening and between Screening and dosing: abnormal Alanine aminotransferase (AST), abnormal aspartate aminotransferase (ALT) or abnormal alkaline phosphatase levels (ALP) >=1.5 x upper limit of normal (ULN); total bilirubin >=1.5 x ULN; or clinically significant laboratory abnormalities or abnormalities which are deemed to interfere with the ability to interpret study data. A repeat is

allowed once to determine eligibility.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-06-2020
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	16-04-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-05-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-07-2020
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	EUCTR2020-000859-12-NL
CCMO	NL73571.056.20

Study results