A Multiple Ascending Dose Study to Evaluate Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ENX-102 at Plasma Steady State in Healthy Volunteers

Published: 01-09-2021
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To evaluate the safety and tolerability of ENX-102 following repeated doses in healthy volunteers

Ethical review	Approved WMO
Status	Completed
Health condition type	Structural brain disorders
Study type	Interventional

Summary

ID

NL-OMON52117

Source
ToetsingOnline

Brief title
MAD to evaluate safety, tolerability, PK and PD of ENX-102 in HV

Condition

- Structural brain disorders

Synonym
Central nervous system disorders

Research involving
Human

Sponsors and support

Primary sponsor: Engrail Therapeutics, Inc
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: ENX-102, GABAA receptor, Selective modulator

Outcome measures

Primary outcome

The safety and tolerability of ENX-102 will be assessed by the following:

• AEs

• Vital signs (2 positional blood pressure and HR, respiratory rate, and

tympanic body temperature)

• 12 lead ECG

• Clinical laboratory tests (hematology, serum chemistry, urinalysis)

• Physical examination

• Pregnancy test (where applicable)

• C SSRS

• MOAA/S

Secondary outcome

Pharmacokinetic Measures:

- Maximum plasma concentration (Cmax)

- Time to reach maximum plasma concentration (Tmax)

- Area under the plasma concentration time curve (AUC) from administration to

the end of dosing (AUC0 t),

- AUC from administration to 24 h after dosing (AUC0 24), AUC extrapolated to

infinite time (AUC0 *),

- Plasma concentration half life (t1/2),

- Terminal rate constant (*z),

- Apparent total clearance of the drug from plasma after oral administration

(CL/F),

- Apparent volume of distribution during terminal phase after non intravenous

administration (Vz/F).

Pharmacodynamic Measures:

• NeuroCart assessments

- Saccadic eye movements, saccadic reaction time (seconds), saccadic peak

velocity (degrees/second), and saccadic inaccuracy (%)

- Smooth pursuit eye movements (percentage of time the eyes of the subject are

in smooth pursuit of the target) (%)

- Adaptive tracking (average performance) (%)

- Body sway (antero posterior sway) (mm)

- Pupil size

- VAS according to Bond and Lader to assess mood, alertness, and calmness (mm)

• Cognitive assessment

o VVLT (Learning and Immediate Recall, Delayed Recall, and Delayed Recognition)

• qEEG

Study description

Background summary

This Phase 1 study will investigate the safety and tolerability, and determine the pharmacokinetic(PK) and pharmacodynamic(PD) profile of ENX-102 in healthy subjects after administration of multiple doses, as part of clinical development before administering this drug to patients.

Study objective

To evaluate the safety and tolerability of ENX-102 following repeated doses in healthy volunteers

Study design

This is a randomized, double blind, placebo controlled, multiple ascending dose study in healthy volunteers.

Intervention

ENX 102 (oral capsules) or placebo (oral capsules) once daily for 12 consecutive days.

Study burden and risks

For this study, healthy male and female participants aged 18 to 55 (inclusive) were chosen because of the absence of potentially confounding disease processes, which will lead to a clearer and more consistent assessment of drug disposition and biological activity. No therapeutic benefit is expected for participants in this study, as is common for most Phase 1 studies with healthy participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Healthy male and female volunteers aged 18 to 55 years, inclusive, at Screening
- Capable of giving written informed consent
- Willing to give written consent to have data entered into "Verified Clinical Trials"
- Female subjects
a. Of non childbearing potential, defined as either permanently sterilized (at least 4 months after surgical sterilization including bilateral salpingectomy, tubal ligation, or oophorectomy with or without hysterectomy) or post menopausal (defined as amenorrhea for 12 consecutive months and documented plasma follicle stimulating hormone level >40 IU/mL; in the event a subject's menopausal status has been clearly established and yet serum follicle stimulating hormone levels are not consistent with a post menopausal status, determination of the subject's eligibility to be included in the study will be at the Investigator's discretion following consultation with the Sponsor), and with a negative pregnancy test at Screening and Day -1; OR
b. Of childbearing potential and willing to use 2 effective methods of contraception (i.e., established method of contraception + condom) or remain abstinent (where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the subject) from Day -1 through 3 months after the last dose of study drug, and with a negative pregnancy test at Screening and Day -1
- Male subjects who, if fertile (defined as post pubertal and not permanently sterile by orchidectomy or vasectomy) must be willing to use a condom or remain abstinent (where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the subject) from Day -1 through 3 months

after the last dose of study drug
- Body mass index of 18 to 35 kg/m2 at Screening
- Willing and able to comply with all study requirements including the following:
a. Reside in the inpatient unit from Day -1 until discharge on Day 13
b. Refrain from strenuous exercise from Day -4 until Day 26
c. Abstain from grapefruit , alcohol , caffeine , or xanthine containing products from Day -4 through Day 26

Exclusion criteria

- Clinically significant abnormality within 2 years of Screening that in the Investigator's opinion may place the subject at risk or interfere with study outcome variables; this includes, but is not limited to, history of or current cardiac, renal, neurologic, gastrointestinal, pulmonary, endocrinologic, hematologic, or immunologic disease or history of malignancy
- Reports having experienced suicidal ideation (Type 4 or 5 on the CSSRS) within 30 days prior to Screening, any suicidal behavior within 2 years prior to Screening (any "Yes" answers on Suicidal Behavior section of C*SSRS), and/or the Investigator assesses the subject to be a safety risk to him/herself or others
- History or evidence of moderate or severe Substance Use Disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders (5th Edition)
- Clinically significant abnormal findings in serum chemistry, coagulation, hematology, or urinalysis results at Screening or Day -1
- Clinically significant abnormal findings in vital sign assessments at Screening or Day -1
- History of hepatitis B or hepatitis C or demonstration of hepatitis B surface antigen or hepatitis C antibody at Screening
- History of HIV infection or demonstration of HIV antibodies at Screening
- Receipt of an investigational drug within 90 days or 5 half*lives, whichever is longer, prior to Day 1 or currently in the follow*up period of another clinical trial at the time of Screening
- Any other condition that, in the Investigator's opinion, might indicate that the subject is unsuitable for the study

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:	Completed
Start date (anticipated):	03-11-2021
Enrollment:	56
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ENX-102
Generic name:	NA

Ethics review

Approved WMO Date:	01-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	28-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	21-07-2022
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	EUCTR2021-004112-25-NL
CCMO	NL78813.056.21

Study results

Date completed:	05-09-2022
Results posted:	13-02-2023

First publication
25-01-2023