SAD & MAD of ABX-002 in HV

No registrations found.

Ethical review	Positive opinion
Status	Suspended
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20666

Source
Nationaal Trial Register

Brief title
CHDR2045

Health condition

Adrenomyeloneuropathy, AMN disease

Sponsors and support

Primary sponsor: Autobahn Therapeutics, Inc.
Source(s) of monetary or material Support: Sponsor

Intervention

Outcome measures

Primary outcome

- Incidence of treatment-emergent AEs, serious adverse events, and suspected, unexpected serious adverse reaction

Secondary outcome

- PK (plasma, urine, CSF)

- PD

- electrocardiograpy effects based on ΔΔQTcF

Study description

Background summary

Adrenoleukodystropy (ALD) is caused by an X-linked inactivating mutation in the ABCD1 gene, encoding for the ALD protein, which is responsible for degradation of very long chain fatty acids (VLCFAs). AMN is the most common phenotype and is characterized by tissue damage in the brain, spinal cord, and in the adrenal, testes, and peripheral nerves due to VLCFA accumulation. Currently, there are no FDA and EMA approved therapies to treat AMN.

ABX-002 is an orally administered prodrug that is hydrolyzed by the intracellular enzyme FAAH, thereby releasing the active metabolite

LL-340001. LL-340001 is a TRβ-selective thyromimetic structurally related to the thyroid hormone T3. Based on preclinical studies, LL340001 might provide therapeutic benefit in AMN by enhancing the expression of ABCD2 (sharing redundancy with ABCD1) and in turn reduced VLCFA levels, thereby correcting the fundamental biochemical abnormality in AMN. In addition, thyroid hormone enhances remyelination by stimulating the differentiation and maturation of oligodendrocyte precursor cells into myelin-producing oligodendrocytes (Fernandez 2004). The TRβ-selective agonists have been shown to promote remyelination in nonclinical models, suggesting the potential for ABX-002 to ameliorate these damaging effects seen in progressive AMN disease (Hartley 2019).

Study objective

Part 1 Single Ascending Dose (SAD)

- To evaluate the safety and tolerability of a single oral dose of prodrug, ABX-002, in healthy adult subjects

Part 2 Multiple Ascending Dose (MAD)

-To evaluate the safety and tolerability of once daily oral doses of ABX-002 administered for 14 days and/or 28 days in healthy adult

subjects

Study design

Day -28 (screening) till EOS

Intervention

SAD: single dose of ABX-002 (oral solution or oral capsule) or placebo (oral solution or capsule)

MAD: multiple doses of ABX-002 (oral solution or oral capsule) or placebo (oral solution or capsule) for either 14 consecutive days or 28

consecutive days

Contacts

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Eligibility criteria

Inclusion criteria

1. Male or female ≥ 18 to ≤ 55 years of age at the time of the Screening Visit.

2. In good health based on medical history, physical examination (including neurological examination), vital sign measurements, and laboratory safety tests obtained at Screening.

3. No clinically significant abnormality on the single ECG performed at Screening and the triplicate ECG performed prior to the first administration of study drug. Single ECG performed at Screening may be repeated once.

Exclusion criteria

1. Estimated creatinine clearance of ≤ 90 mL/min based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Levey 2009).

2. History or evidence of any of the following: myocardial infarction; cardiac valvulopathy; cardiac surgery revascularization (coronary artery bypass grafting or percutaneous transluminal coronary angioplasty); unstable angina; cerebrovascular accident, stroke, or transient ischemic attack; pacemaker; atrial fibrillation, flutter, or nonsustained or sustained VT; pulmonary arterial hypertension; sick sinus syndrome, second- or third-degree atrioventricular (AV) block; uncontrolled hypertension; congestive heart failure; personal or family history of sudden death or long QT syndrome; unexplained syncope or syncope within the last 3 years regardless of etiology; or history of hypokalemia.

3. Screening Holter monitor (24 hours) shows nonsustained VT, SVT lasting > 10 beats in a run or > 4 runs, atrial fibrillation, atrial flutter, or a pause > 4 seconds.

4. Mean pulse < 50 or > 100 bpm, mean systolic blood pressure >140 mm Hg, or mean diastolic blood pressure > 90 mm Hg at Screening measured in triplicate using a calibrated digital device. If the mean blood pressure

exceeds the limits above, an additional set of blood pressure measurements will be obtained, and the subject may be included if pulse and BP parameters are within the permitted boundaries.

5. Troponin T out of the normal laboratory range at time of the Screening Visit.

6. Consumption of excessive amounts of caffeine, defined as > 4 servings of coffee, tea, cola, or other caffeinated beverages per day (1 serving is approximately 120 mg of caffeine). Refusal to abstain from caffeine-containing foods or caffeinated beverages (eg, coffee, tea, cola, energy drinks) 5 days prior to Day -1 through discharge from the CRU after the final administration of study drug.

7. Refusal to abstain from grapefruit-containing foods or beverages or Seville orange-containing foods or beverages 14 days prior to Day -1 through the Follow-Up Visit

8. Refusal to abstain from consumption of cruciferous vegetables (eg, kale, broccoli, watercress, collard greens, kohlrabi, brussels sprouts, mustard greens) or charbroiled meats (meat grilled over any heat source with black

marks) ≤ 7 days prior to Day -1 through the Follow-Up Visit

9. Abnormal thyroid function tests (thyroid-stimulating hormone [TSH], triiodothyronine, free thyroxine [FT4]) out of the normal laboratory value ranges at the time of the Screening Visit.

10. Aspartate aminotransferase, alanine aminotransferase, or gamma-glutamyl transferase > 1.5 times the upper limit of normal at the time of the Screening Visit and at Day -1.

Study design

Design

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

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	25-10-2021
Enrollment:	96
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion

Date:	22-10-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 50699
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9828
CCMO	NL78983.056.21
OMON	NL-OMON50699

Study results

Summary results
N.A.