A Phase 1 Study Evaluating the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of IW-6463 when Administered to Healthy Volunteers as Single Ascending Doses with a Food Interaction Cohort, and as Multiple Ascending Doses

Published: 04-01-2019
Last updated: 12-04-2024

Stage 1* To assess the safety and tolerability of single-ascending-dose levels of IW-6463 when administered to healthy subjectsStage 2* To assess the safety and tolerability of multiple-ascending-dose levels of IW-6463 when administered to healthy…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mental impairment disorders
Study type	Interventional

Summary

ID

NL-OMON47937

Source
ToetsingOnline

Brief title
IW 6463 in healthy subjects as a SAD, MAD and Food interaction

Condition

- Mental impairment disorders

Synonym
Alzheimer's disease, Dementia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Alzheimer's Disease, Dementia

Outcome measures

Primary outcome

Stage 1

* Number of subjects with treatmentemergent adverse events (TEAEs) in the

IW-6463 dose-level cohorts vs the (pooled) placebo group.

Stage 2

* Number of subjects with TEAEs in the IW-6463 dose-level cohorts vs the

(pooled) placebo group.

Stage 3

* Number of subjects with TEAEs in the fed vs fasted dosing period.

* Plasma concentration of IW-6463 after single-dose administration under fed vs

fasted conditions.

Secondary outcome

Not applicable

Study description

Background summary

Dementia and cognitive impairment are large and growing health problems in developed and developing countries.A therapeutic intervention that attenuates cognitive decline, or preserves a patient*s current cognitive and functional capacities, or improves either cognitive or functional
capacities, would be of great benefit for patients and their families and caregivers. This study is being conducted to investigate the viability of developing IW-6463 as a potential therapy in patients. As described in the IW-6463 IB, nonclinical data suggest that IW-6463 may offer a novel approach to potentially improve some of the deficits associated with various forms of dementia.

Study objective

Stage 1
* To assess the safety and tolerability of single-ascending-dose levels of IW-6463 when administered to healthy subjects

Stage 2
* To assess the safety and tolerability of multiple-ascending-dose levels of IW-6463 when administered to healthy subjects for up to 14 days

Stage 3
* To assess the safety and tolerability of a single dose of IW-6463 when administered to healthy subjects in fed vs fasted states.
* To explore the effects of food on IW-6463 pharmacokinetics (PK)

Study design

* Stage 1 will evaluate single-ascending-dose levels of study drug (ie, IW-6463 or placebo) in healthy adults using a randomized, double-blind, sequential-group design.
* Stage 2 will evaluate multiple-ascending-dose levels (1 dose level per cohort) of study drug administered to healthy adults (*65 years) for up to 14 days using a randomized, double-blind, sequential-group design.
* Stage 3 will investigate the effect of food on IW-6463 PK by administering a single dose to healthy adults using an open-label, randomized, 2-period, 2-treatment (fed vs fasted conditions), crossover design.

Intervention

* Orally administered IW-6463 Tablets at doses ranging from 0.3 mg/day to not

more than 50 mg/day
* Orally administered Placebo to Match IW-6463 Tablets

Study burden and risks

Healthy subjects will be included in this study. No clinical benefit is to be expected for these participants. The subjects will, however, receive financial compensation. As Study C6463-101 represents the FIH study of IW-6463, the safety profile of IW-6463 in
humans is not known. Nonclinical data indicate that the risk of IW-6463 to human subjects is low when administered at the dose levels planned for this study. Information regarding the potential benefits and risks and reasonably expected treatment-emergent adverse events (TEAEs)
based on nonclinical data can be found in the IW-6463 IB. To minimize risk to subjects, sentinel dosing will be utilized in Stage 1 in which the first
2 subjects (1 randomized to IW-6463 and 1 to placebo) in Cohorts 1 and 2 will be dosed *24 hours in advance of the remaining subjects in the respective cohort. Dosing of the remaining subjects within the respective cohort will proceed (5 to IW-6463; 1 to placebo) on the basis that
no adverse events (AEs) of concern are reported (eg, serious adverse events [SAEs] and/or severe AEs considered related to study drug), according to the judgment of the Investigator and the Sponsor Medical Monitor. Dosing in each subsequent dose-level cohort will
proceed sequentially after a safety review of the preceding cohort(s) has been conducted by the Trial Safety Committee. This FIH stage in healthy volunteers will provide safety, tolerability, and PK data pertaining to oral
administration of IW-6463 in the fasted versus fed states. These data will inform key dosing instructions for future studies and, depending on the results, will guide the dosing regarding food in future trials.

Contacts

Public
Cyclerion Therapeutics, Inc.

Binney Street 301
Cambridge Massachusetts MA 02142
US
Scientific
Cyclerion Therapeutics, Inc.

Binney Street 301
Cambridge Massachusetts MA 02142
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Signed an ICF before any study-specific procedures are performed.
2. Age is *18 and <65 years at the Screening Visit.
3. Body mass index is *18.5 and <32 kg/m2 at the Screening Visit.
4. Ambulatory, in good health and no clinically significant findings on a physical examination,
12-lead ECG, alcohol breathalyzer, and clinical laboratory tests (ie, serum chemistry,
hematology, coagulation, urine drug screen, and urinalysis) after signing the ICF but before
receiving the dose of study drug.
5. Screening results are negative for the hepatitis panel (hepatitis B surface antigen [HBsAg],
the antihepatitis C virus [HCV]), and the human immunodeficiency virus (HIV) antibody.

Exclusion criteria

1. Participated in any clinical study or treated with any investigational drug or device within 28 days prior to Screening.
2. Clinically significant manifestation of metabolic; hepatic; renal; hematological; pulmonary; cardiovascular; gastrointestinal; endocrinological; musculoskeletal; dermatological; urogenital; eye, ear, nose, and/or throat; psychiatric (including history of clinical depression or suicidal ideation, any cognitive impairment or dementia); or neurological disorder that, in the opinion of the Investigator, precludes the subject from participating in the study.
3. Lymphoma, leukemia, or any malignancy within the past 5 years. Exception:

Basal cell or squamous epithelial carcinomas of the skin that have been resected with no evidence of
metastatic disease for 3 years.
4. Clinically significant hypersensitivity or allergy to any of the inactive ingredients contained in the active or placebo drug products.
5. Active alcoholism or drug addiction during the 12 months before the Screening Visit or has a positive urine drug screen or alcohol test (see Section 8.1.7.2) at the Screening Visit or at
Check-in to the Study Center.
6. 12-lead ECG at the Screening Visit demonstrating severe bradycardia (HR <40 beats per minute) or average QT interval corrected for HR using Fridericia*s formula (QTcF) *450 msec for men or *470 msec for women.
7. Family history of short QT syndrome or long QT syndrome.
8. Elevated levels (ie, >1.5× the upper limit of normal as defined by the laboratory) at the Screening Visit or at Check-in of alanine aminotransferase, aspartate aminotransferase, or
creatinine.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-01-2019
Enrollment:	138
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	IW-6463
Generic name:	NA

Ethics review

Approved WMO Date:	04-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-01-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-07-2019

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	EUCTR2018-003694-99-NL
ClinicalTrials.gov	NCT03856827
CCMO	NL67677.056.18