A Phase 1 Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Multiple Ascending Doses of ALKS 7119 in Healthy Adults

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Primary:* Evaluate the safety and tolerability of ALKS 7119 following oral administration of multiple ascending doses of ALKS 7119 in healthy male and female adultsSecondary:* Evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of ALKS 7119...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON43047

Source
ToetsingOnline

Brief title
Multiple ascending doses study of ALKS 7119

Condition

- Neurological disorders NEC
- Dementia and amnestic conditions

Synonym
Alzheimer's disease, Dementia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ALKS7119, Pharmacodynamics, Pharmacokinetics, Safety

Outcome measures

Primary outcome

Safety and tolerability: Evaluation of safety will be based on the occurrence of adverse events (AEs), vital signs, results of clinical laboratory tests electrocardiogram (ECG) parameters, real-time ECG parameters. Reported AE terms will be coded using the Medical Dictionary for Regulatory Activities (MedDRA® version 19.0 or higher) preferred terms and system organ classes.

Secondary outcome

Pharmacokinetics: Concentrations of ALKS 7119 will be quantified in plasma samples collected for PK evaluation. Noncompartmental PK analyses will be performed to estimate the PK parameters.

At a minimum, the following PK parameters will be determined for ALKS 7119, as applicable:

* Maximum plasma concentration (Cmax) of ALKS 7119 on Day 1 and Day 14

* Area under the concentration-time curve from time zero to the last quantifiable time interval (AUClast) on Day 1 and Day 14

* Area under the concentration-time curve over the 24-hour dosing interval (AUC24h) of ALKS 7119 on Day 1 and Day 14

* Area under the concentration-time curve from time zero to infinity (AUC*)

after the first dose on Day 1

* Time to Cmax (tmax) of ALKS 7119 on Day 1 and Day 14

* Terminal elimination half-life (t*) of ALKS 7119 on Day 1 and Day 14

* Trough plasma concentration (Ctrough) on Day 1 through Day 14

* Accumulation ratio (Day 14/Day 1 AUC24h ratio)

Dose proportionality assessment and additional PK analyses may be performed as

appropriate.

Study description

Background summary

Emerging studies point to a potential role for NMDA antagonists in treating behavioral symptoms associated with Alzheimer*s disease, including agitation [Cummings, 2014;Wilcock, 2008]. There are currently no approved drugs in the US for treating these symptoms, which diminish quality of life for patients and caretakers and correlate with a poorer disease prognosis. Developing drugs for this indication therefore represents a significant clinical need. As a low-affinity antagonist at the NMDA receptor, Alkermes postulates that ALKS 7119 may be applicable for this purpose.

Study objective

Primary:
* Evaluate the safety and tolerability of ALKS 7119 following oral administration of multiple ascending doses of ALKS 7119 in healthy male and female adults

Secondary:
* Evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) of ALKS 7119 following oral administration of multiple ascending doses of ALKS 7119 in healthy male and female adults

Study design

This is a Phase 1, single-center, randomized, double-blind, placebo-controlled, MAD study of ALKS 7119 in healthy adults. This study will evaluate the safety,

tolerability, PK, and PD of ALKS 7119 following multiple ascending doses. The study will include at least 4 cohorts, with each cohort representing a different dose level. Gender will be approximately equally balanced across cohorts (with a minimum of one-third female subjects).
Potential subjects will be screened up to 21 days prior to administration of study drug. Dosing of cohorts will be separated by at least
7 days to allow adequate time for a review of all safety, PD, and PK data from the most recently dosed cohort.
The study duration for a given subject is expected to be up to 6 weeks, which includes up to 3 weeks for screening, an inpatient
stay from Day -1 to Day 215 and a follow-up visit on Day 21 (+3 days).

Intervention

The subjects will receive multiple doses of ALKS 7119 or placebo.

Study burden and risks

There is no health benefit for participants. Risk is considered minimal. Burden consists of time investment and life style restrictions.

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. Is willing and able to provide informed consent
2. Is capable of understanding and complying with the protocol
3. Is male or female adult and *18 and *45 years of age, inclusive, at screening (Visit 1)
4. Has a body mass index *18.0 and *32.0 kg/m2 at screening
5. Agrees to use an acceptable method of contraception from 30 days prior to screening and for 90 days after any study drug administration, or must be surgically sterile or post-menopausal (if female)

Exclusion criteria

1. Clinically significant medical condition or observed abnormalities, in the opinion of the investigator (including, clinically significant physical examination finding, vital sign result, ECG result, laboratory or urinalysis test result) and/or any other finding that, in the investigator*s judgment, could potentially compromise subject safety, or PK or PD evaluation, or affect the subject*s ability to adhere to the protocol visit schedule, or fulfill visit requirements
2. Female subject that is currently pregnant or breastfeeding, or plans to become pregnant or begin breastfeeding at any point during the study and for 90 days after any study drug administration
3. Has a history of intolerance or hypersensitivity to dextromethorphan or any dextromethorphan-containing product
4. Has had a clinically significant illness in the 30 days prior to first study drug administration (Day 1)
5. Has a positive drug screen for at screening (Visit 1) or upon admission (Day -1)
6. Has a positive breath test for alcohol at screening (Visit 1) or upon admission (Day -1)
7. Has a positive serology test for hepatitis B virus surface antigen (HBsAg), hepatitis B virus core antibody (HBcAb), hepatitis C virus antibody (HCVAb), or human immunodeficiency virus antibody (HIVAb) at screening (Visit 1)
8. Has a clinically significant lifetime history of suicidal ideation or suicidal behavior and/or poses a current (within past year) suicide risk
9. Has used any prescription or over-the-counter medication, including herbal remedies and nutritional supplements (except vitamins), within 7 days prior to screening (Visit 1) or admission (Day -1)
10. Has ingested any alcohol, caffeine or xanthine within 24 hours prior to inpatient

admission (Day -1), or excessive caffeine consumption (defined as *800 mg per day) at screening (Visit 1)
11. Has used any product containing nicotine within 30 days prior to admission (Day -1)
12. Has participated in a clinical trial of an investigational product within 3 months prior to screening (Visit 1) or participated in more than four investigational drug studies within 1 year prior to screening (Visit 1)
13. Has previously participated in a clinical trial with ALKS 7119

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):	21-06-2016
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ALKS 7119
Generic name:	ALKS 7119

Ethics review

Approved WMO

Date:	01-06-2016

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-06-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-07-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-08-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-11-2016
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	EUCTR2016-001905-18-NL
CCMO	NL57772.056.16