ISRCTN98204977 https://doi.org/10.1186/ISRCTN98204977

A study in healthy subjects to see the effects of the test medicine ALKS 2680 in single and multi-dose regimen

Submission date
14/10/2022

Recruitment status
No longer recruiting

Registration date
17/10/2022

Overall study status
Completed

Last Edited
05/06/2024

Condition category
Nervous System Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
This is a clinical study to assess how safe and well tolerated an investigational drug (ALKS 2680) is in healthy adults and adults with narcolepsy or idiopathic hypersomnia, as well as to understand how food and different formulations (recipes) of ALKS 2680 affect the time it takes the study drug to enter the bloodstream and to be removed from the body.

Who can participate?
Healthy adults or adults with a narcolepsy or idiopathic hypersomnia diagnosis aged 18-65 years.

What does the study involve?
The study is broken down into 6 parts.
Part 1 is designed to assess the effect of a single dose of ALKS 2680 in healthy participants. Participants will have 3 study visits which include a screening, a treatment period with 4 overnight stays and a safety follow-up.
Part 2 is designed to assess the effect of multiple daily doses of ALKS 2680 in healthy participants. Participants will have 3 study visits which includes a screening, a treatment period with 12 overnight stays and a safety follow-up.
Part 3 is designed to assess the effect of food and different formulations (recipes) of the drug on how much and how fast the study drug gets into the bloodstream and how fast it is removed from the body. Participants will have 3 study visits, including a screening, a treatment period with 10 overnight stays and a safety follow-up.
Part 4 is designed to assess the safety and tolerability of ALKS 2680 in individuals with narcolepsy type 1 (NT1). Participants will have 3 study visits, including a screening, a treatment period with 10 overnight stays and a safety follow-up. At screening, participants will undergo a washout
from their current prescription medications of at least 14 days.
Part 5 is designed to assess the safety and tolerability of ALKS 2680 in individuals with narcolepsy type 2 (NT2). Participants will have 3 study visits, including a screening, a treatment period with 10 overnight stays and a safety follow-up. At screening, participants will undergo a washout

from their current prescription medications of at least 14 days.
Part 6 is designed to assess the safety and tolerability of ALKS 2680 in individuals with idiopathic hypersomnia (IH). Participants will have 3 study visits, including a screening, a treatment period with 10 overnight stays and a safety follow-up. At screening, participants will undergo a washout from their current prescription medications of at least 14 days.

What are the possible benefits and risks of participating?
This is a phase 1study, and participants will be administered the study drug for research purposes only. This trial may help reveal important scientific knowledge that could contribute to the development of a drug.
As with all interventional studies, the drug treatment may involve risks that are known as well as risks that are currently unknown. Participants will be carefully monitored for any side effects; however, not all of the side effects that the study drug may have are known.

Where is the study run from?
This is a multi-center study run from Australia and United States

When is the study starting and how long is it expected to run for?
April 2022 to February 2024

Who is funding the study?
Alkermes, Inc. (USA)

Who is the main contact?
clinicaltrials@alkermes.com

Contact information

Type(s)
Public

Contact name
Ms Clinical Operations

Contact details
900 Winter Street
Waltham
United States of America
02451
+1 571-599-2702
Clinicaltrials@alkermes.com

Type(s)
Scientific

Contact name
Ms Clinical Operations

Contact details
900 Winter Street
Waltham

United States of America
02451
+1 571-599-2702
clinicaltrials@alkermes.com

Type(s)
Principal investigator

Contact name
Ms Clinical Operations

Contact details
Bright Building, Level 5
Corner High and Avoca Street
Randwick
Australia
NSW 2031
+1 571-599-2702
clinicaltrials@alkermes.com

Additional identifiers

Protocol serial number
2022-08-0914

Study information

Scientific Title
A single and multiple ascending dose study to evaluate the safety, tolerability and PK of ALKS 2680 in healthy subjects and subjects with hypersomnia

Study objectives
Current study hypothesis:
Study to assess safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple daily doses of ALKS 2680 in healthy subjects and subjects with narcolepsy or idiopathic hypersomnia. Additionally, the relative BA and food effect of the new formulation will be evaluated.

Previous study hypothesis as of 16/03/2023:
Study to assess safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple daily doses of ALKS 2680. Additionally, the relative BA and food effect of the new formulation will be evaluated.

Previous study hypothesis:
Study to assess the safety, tolerability and pharmacokinetics of single ascending and multiple ascending doses of ALKS 2680. Additionally, the relative bioavailability and food effect of new formulations will be evaluated.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/10/2022, Bellberry HREC (123 Glen Osmond Road, Eastwood SA 5063, Australia; +61 9 8361 3222; bellberry@bellberry.com.au), ref: 2022-08-0914

Study design
Multi-centre randomized double-blinded placebo-controlled study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Phase 1 drug study

Interventions
Current interventions as of 11/01/2024:

Part 1 SAD: Participants will be randomized to receive oral ALKS 2680 or placebo for 1 day. Part 2 MAD: Randomized to receive oral ALKS 2680 or placebo for 10 days.
Part 3 Relative Bioavailability and Food effect: Patients will be randomized to receive new formulations of ALKS 2680 in one of two sequences in a cross-over design.
Parts 4-6 POC: Randomized to receive oral ALKS2680 at 1 of 3 dose levels or placebo for days 1, 3, 5, 7 of the in-clinic stay separated by approximately 48 hours of washout

Randomisation Process: password protected electric file Interventions Duration:
Part 1: Screening: 28 days Treatment: 3 days Follow-up: 1 day (7 days after last dose)
Part 2: Screening: 28 days Treatment: 12 days Follow-up: 1 day (5 days after last dose)
Part 3: Screening: 28 days treatment: 9 Follow-up: 1 day (5 days after last dose)
Parts 4-6: Screening: 28 Days Treatment: 11 days Follow-up: 1 day (7 days after last dose)

———

Previous interventions:

Part 1 SAD: Participants will be randomized to receive oral ALKS 2680 or placebo for 1 day.
Part 2 MAD: Randomized to receive oral ALKS 2680 or placebo for 10 days.
Part 3 Relative Bioavailability and Food effect: Patients will be randomized to receive new formulations of ALKS 2680 in one of two sequences in a cross-over design.

Randomisation Process: password protected electric file
Interventions Duration:
Part 1: Screening: 28 days Treatment: 3 days Follow-up: 1 day (7 days after last dose)
Part 2: Screening: 28 days Treatment: 12 days Follow-up: 1 day (5 days after last dose)
Part 3: Screening: 28 days treatment: 9 Follow-up: 1 day (5 days after last dose)

Intervention Type
Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)
ALKS 2680

Primary outcome(s)
Current primary outcome measure as of 11/01/2024:

Parts 1,2,3,4,5,6
1. Incidence of treatment-emergent adverse events assess throughout the trial (enrollment to study follow-up)

_____

Previous primary outcome measure:

Parts 1,2,3
1. Incidence of treatment-emergent adverse events assess throughout the trial (enrollment to study follow-up)

Key secondary outcome(s))
Current secondary outcome measures as of 11/01/2024:

Part 1 & 3
1. Levels of ALKS 2680 in blood measured as Cmax , Tmax (Day 1), AUC (over 12 hours), T-half, CL /F, and Vz/F using non-compartmental methods

Part 2
1. Levels of ALKS 2680 in blood and urine measured as Cmax , Tmax (Day 1), AUC (over 7 days) T-half, CL/F, and Vz/F using non-compartmental methods

Parts 4 & 6
1. Levels of ALKS 2680 in blood and urine measured as Cmax , Tmax (Day 1), AUC (over 8 hours) T- half, CL/F, and Vz/F using non-compartmental methods
2. Change from Baseline to post-dose on dosing days in the average sleep latency across the first 4 sessions of the Maintenance of Wakefulness Test (MWT)

_____

Previous secondary outcome measures:

Part 1 & 3
1. Levels of ALKS 2680 in blood measured as Cmax , Tmax (Day 1), AUC (over 12 hours), T-half, CL /F, and Vz/F using non-compartmental methods

Part 2
1. Levels of ALKS 2680 in blood and urine measured as Cmax , Tmax (Day 1), AUC (over 7 days) T-half, CL/F, and Vz/F using non-compartmental methods

Completion date
01/05/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 11/01/2024:

1. Is a healthy male or female aged 18 to 65 years at the time of informed consent.
2. Is willing and able to provide informed consent before study participation, as required by local regulations and Independent Ethics Committee (IEC) requirements.
3. Is willing and able, in the opinion of the Investigator, to understand and comply with protocol requirements, including adherence to contraception requirements.
4. Has a body mass index (BMI) ≥18 and ≤30 kg/m² at Screening.

Parts 4-6 Only
6. Has a diagnosis of NT1, NT2, or IH according to ICSD-3 guidelines.
7. Has residual EDS (ie, ESS total score >10, referencing the week immediately prior) at Visit 2.
8. Is willing and able to discontinue any medications prescribed for the management of narcolepsy or IH symptoms including EDS and/or cataplexy at least 14 days (or 5 half-lives, whichever is longer) prior to Visit 2 to enable sufficient washout and resolution of any withdrawal symptoms.
9. Has a BMI ≥18 and ≤40 kg/m² at Screening.

_____

Previous inclusion criteria:

1. Is a healthy male or female aged 18 to 65 years at the time of informed consent.
2. Is willing and able to provide informed consent before study participation, as required by local regulations and Independent Ethics Committee (IEC) requirements.
3. Is willing and able, in the opinion of the Investigator, to understand and comply with protocol requirements, including adherence to contraception requirements.
4. Has a body mass index (BMI) ≥18 and ≤30 kg/m² at Screening.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment

Key exclusion criteria

Current exclusion criteria as of 11/01/2024:

1. Is currently enrolled in another clinical study or used any investigational drug or device within 30 days prior to Screening.
2. Is currently pregnant, breastfeeding, or is planning to become pregnant during the study.
3. Does not have a history or presence of any clinically significant (treated or untreated) illness, disease, abnormality, behavioral or psychiatric disorder, or surgical procedure that, in the opinion of the Investigator, might compromise subject safety, interfere with any study assessment, or affect the subject's ability to complete the trial.
4. Has a positive alcohol breath test or urine drug screen for drugs of potential abuse at In-clinic Admission.
5. Has a history or presence at Screening of any clinically significant (treated or untreated) illness, disease, abnormality, behavioral or psychiatric disorder or surgical procedure that, in the opinion of the Investigator, might compromise subject safety, interfere with any study assessment, or affect the subject's ability to complete the trial.
6. Has a history or presnce at Screening of any significant cardiovascular disease (eg, myocardial infarction, ischemic heart disease, cardiac failure, arrhythmia).
7. Has a corrected QT interval (Fridericia correction; QTcF) >450 milliseconds (msec) if male and >470 msec if female, PR interval >210 msec, or any other ECG finding at Screening or upon admission, confirmed by repeat testing, that, in the opinion of the Investigator, might compromise subject safety.
8. Has a history of left bundle branch block or evidence of same on ECG at Screening or Baseline.
9. Has persistent systolic BP >[140] or <[90] mmHg or diastolic BP >[90] or <[50] mmHg at Screening or Baseline, or history of orthostatic hypotension.
10. Has persistent HR <45 beats/min or >100 beats/min at Screening or Baseline.
11. Is employed by Alkermes, the contract research organization (CRO), or study site (permanent, temporary contract worker, or designee responsible for the conduct of the study) or is immediate family (ie, a spouse, parent, sibling, or child, whether biological or legally adopted) of an Alkermes, CRO, or study site employee.
12. Consumes more than 400 mg of caffeine (ie, >5 cups of coffee) per day or has substantial changes in caffeine consumption in the 30 days prior to Screening.
13. Consumes more than 20 grams of alcohol (ie, >2 "standard" drinks in Australia) per day or has substantial changes in alcohol consumption in the 30 days prior to Screening.
14. Consumes nicotine daily (ie, ≥1 cigarette, vaping or chewing tobacco, nicotine patch or gum) or has substantial changes in nicotine consumption in the 30 days prior to Screening.
15. Consumes cannabis or cannabis-derived compounds (eg, marijuana cigarettes, vaping, edibles, beauty and skincare products, or oils containing cannabidiol [CBD] and/or tetrahydrocannabinol [THC]) more than 3 times per month or has substantial changes in cannabis consumption in the 30 days prior to Screening.
16. Has a substance use disorder according to Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition; DSM-5) guidelines, including use of alcohol, nicotine, cannabis, narcotics, or any illicit substance.
17. Has a positive alcohol breath test or urine drug screen for drugs of potential abuse at In-clinic Admission.
18. Has active suicidal ideation or any history of suicidal behavior; or has a "Yes" to any of the five yes/no questions on the Columbia Suicide Severity Rating Scale (C-SSRS) for the period within 12 months up to and at the time of Screening.
19. Is currently taking any prescription or over-the-counter (OTC) medications or has taken any

medications in the past 14 days or 5 half-lives, whichever is longer, immediately prior to In-clinic Admission.

Subjects in Parts 1-3 Only
20. Has EDS (ie, ESS total score >10) at Screening.

Subjects in Parts 4-6 Only
21. Has any clinically significant illness or disease, other than NT1, NT2, or IH, associated with excessive sleepiness, that, as judged by the Investigator, has the potential to compromise subject safety or interfere with any study assessment.

_____

Previous exclusion criteria:

1. Is currently enrolled in another clinical study or used any investigational drug or device within 30 days prior to Screening.
2. Is currently pregnant, breastfeeding, or is planning to become pregnant during the study.
3. Does not have a history or presence of any clinically significant (treated or untreated) illness, disease, abnormality, behavioral or psychiatric disorder, or surgical procedure that, in the opinion of the Investigator, might compromise subject safety, interfere with any study assessment, or affect the subject's ability to complete the trial.
4. Has a positive alcohol breath test or urine drug screen for drugs of potential abuse at In-clinic Admission.
5. Has a history or presence at Screening of any clinically significant (treated or untreated) illness, disease, abnormality, behavioral or psychiatric disorder or surgical procedure that, in the opinion of the Investigator, might compromise subject safety, interfere with any study assessment, or affect the subject's ability to complete the trial.
6. Has a history or presence at Screening of any significant cardiovascular disease (eg, myocardial infarction, ischemic heart disease, cardiac failure, arrhythmia).
7. Has a corrected QT interval (Fridericia correction; QTcF) >450 milliseconds (msec) if male and >470 msec if female, PR interval >210 msec, or any other ECG finding at Screening or upon admission, confirmed by repeat testing, that, in the opinion of the Investigator, might compromise subject safety.
8. Has a history of left bundle branch block or evidence of same on ECG at Screening or Baseline.
9. Has persistent systolic BP >[140] or <[90] mmHg or diastolic BP >[90] or <[50] mmHg at Screening or Baseline, or history of orthostatic hypotension.
10. Has persistent HR <45 beats/min or >100 beats/min at Screening or Baseline.
11. Is currently pregnant, breastfeeding, or is planning to become pregnant during the study.
12. Is employed by Alkermes, the contract research organization (CRO), or study site (permanent, temporary contract worker, or designee responsible for the conduct of the study) or is immediate family (ie, a spouse, parent, sibling, or child, whether biological or legally adopted) of an Alkermes, CRO, or study site employee.
13. Is currently enrolled in another clinical study or used any investigational drug or device within 30 days prior to Screening.
14. Consumes more than 400 mg of caffeine (ie, >5 cups of coffee) per day or has substantial changes in caffeine consumption in the 30 days prior to Screening.
15. Consumes more than 20 grams of alcohol (ie, >2 "standard" drinks in Australia) per day or has substantial changes in alcohol consumption in the 30 days prior to Screening.
16. Consumes nicotine daily (ie, ≥1 cigarette, vaping or chewing tobacco, nicotine patch or gum) or has substantial changes in nicotine consumption in the 30 days prior to Screening.
17. Consumes cannabis or cannabis-derived compounds (eg, marijuana cigarettes, vaping,

edibles, beauty and skincare products, or oils containing cannabidiol [CBD] and/or tetrahydrocannabinol [THC]) more than 3 times per month or has substantial changes in cannabis consumption in the 30 days prior to Screening.
18. Has a substance use disorder according to Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition; DSM-5) guidelines, including use of alcohol, nicotine, cannabis, narcotics, or any illicit substance.
19. Has a positive alcohol breath test or urine drug screen for drugs of potential abuse at In-clinic Admission.
20. Has active suicidal ideation or any history of suicidal behavior; or has a “Yes” to any of the five yes/no questions on the Columbia Suicide Severity Rating Scale (C-SSRS) for the period within 12 months up to and at the time of Screening.
21. Is currently taking any prescription or over-the-counter (OTC) medications or has taken any medications in the past 14 days or 5 half-lives, whichever is longer, immediately prior to In-clinic Admission.

Date of first enrolment
24/10/2022

Date of final enrolment
01/05/2024

Locations

Countries of recruitment
Australia

United States of America

Study participating centre
Scientia Clinical Research Limited
Bright Building, Level 5
Corner High and Avoca Street
Randwick
Australia
NSW 2031

Study participating centre
Woolcock Institute of Medical Research
431 Glebe Point Road
Glebe
Australia
NSW 2037

Study participating centre

AISH Flinders University
Level 2A Mark Oliphant Building
5 Laffer Drive
Bedford Park
Adelaide
Australia
SA 5042

Study participating centre
Biotrial
130 Norfolk Street
Newark
United States of America
NJ 07103

Sponsor information

Organisation
Alkermes (United States)

ROR
https://ror.org/038hqfn26

Funder(s)

Funder type
Industry

Funder Name
Alkermes

Alternative Name(s)
Alkermes plc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
Ireland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to intellectual property

IPD sharing plan summary
Not expected to be made available