A Randomized, Double-Blind, Placebo-Controlled, Single Ascending Dose Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of ALKS 6610 with a Pilot Evaluation of Food Effect in Healthy Adult Subjects

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The objective of the study is to evaluate safety, tolerability, and pharmacokinetics (PK) of ALKS 6610 after single ascending oral doses in healthy adult subjects.

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50062

Source
ToetsingOnline

Brief title
ALKS 6610 in healthy adults

Condition

- Other condition

Synonym
Chronic pain

Health condition

Pain

Research involving
Human

Sponsors and support

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

Intervention

Keyword: chronic pain, FIH, opioids

Outcome measures

Primary outcome

Tolerability / Safety Endpoints

Pharmacokinetic Endpoints

Secondary outcome

Pharmacodynamic Endpoints

Study description

Background summary

Chronic pain of moderate to severe intensity occurs in 19% of adult Europeans, seriously affecting the quality of their social and working lives (Breivik et al., 2006). More than 100 million people in the United States (~31% of the adult population) are affected by chronic pain (National Research Council 2011). Opioids are effective treatments prescribed for acute and chronic pain. An estimated 20% of patients presenting to physician offices with non-cancer pain or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription (Daubresse et al., 2013). However, opioid pain medications are associated with serious risks including overdose, respiratory depression, constipation, sedation, and opioid use disorder. As such, there is an unmet need for well-tolerated and effective therapies, including opioids with improved safety characteristics, for the management of pain, especially chronic

pain. Additionally, central to the abuse-related side effects of opioid analgesics is their rapid entry into the brain and activation of brain circuits underlying reward and reinforcement (Volkow et al., 2000). Opioid analgesics with slower or reduced brain exposure have been postulated to have lower potential of abuse and addiction (Miyazaki et al., 2017). ALKS 6610 was designed to be a partial μ-opioid receptor (MOR) agonist with a preference toward G-protein coupled intracellular signalling, with low levels of β-arrestin recruitment and a predicted reduced rate of brain penetration. The mechanism of action and available pharmacology data suggest that ALKS 6610 has the potential to improve the treatment of pain by providing opioid-like analgesia with an improved safety profile, including lower abuse potential and reduced risk of respiratory depression, compared to currently approved opioid agonists.

This is the first study with ALKS 6610 in humans, designed to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of single ascending doses with a pilot evaluation of food effect. The study results will be used to support further clinical development of ALKS 6610.

Study objective

The objective of the study is to evaluate safety, tolerability, and pharmacokinetics (PK) of ALKS 6610 after single ascending oral doses in healthy adult subjects.

Study design

This study will be a randomized, single-centre, double-blind, placebo-controlled single ascending dose (SAD) study in healthy adult subjects to evaluate the safety, tolerability, PK, and PD of ALKS 6610.

Intervention

Capsules of 25mg, 75mg, 150mg, 300mg, 600mg, 900mg, 1200mg ALKS 6610 or placebo.

Study burden and risks

The risks associated with the administration of ALKS 6610 to humans have not yet been identified, since this will be the first administration in humans. All study drug administrations will be performed ¡n the clinic under medical supervision. The proposed FIH study consists in a single dose administration, with close monitoring of participants' vital functions during 96h following administration. The monitoring of vital function includes the monitoring of respiratory rate, oxygen saturation, end-tidal CO2, ECG, pupil

size, blood pressure and heart rate. Thus, the subjects will be closely monitored for any adverse signs during all dose levels.
Therefore careful observation and medical management will minimize any associated risk in this study. For all dose levels, the first administrations will be dosed using a sentinel approach: the first two subjects will be randomized to receive 1 placebo and 1 active and dosed with a 24 hour observation period prior to dosing the remaining subjects of the dose level. In case of an emergency suggesting opioid overdose with ALKS 6610, supportive care measures with or without naloxone followed by close monitoring for several hours are indicated.

Healthy subjects in the current study fall in a low risk category for complications of COVID-19, the disease caused by the SARSCoV-2 virus. To prevent SARS-CoV-2 infections among trial participants, measures and procedures based on the advice issued by the Dutch Centre for Infectious Disease Control (RIVM) and COVID-19 measures declared by the Dutch government will be adhered to as outlined in CHDR SOP GGECOVID.

Contacts

Public
Alkermes, Inc

Winter Street 852
Waltham MA 02451
US
Scientific
Alkermes, Inc

Winter Street 852
Waltham MA 02451
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed informed consent prior to any study-mandated procedure
2. Ability to communicate well with the Investigator in the Dutch language and willing to follow the procedures and comply with study restrictions as outlined in the protocol
3. Male or female age >=18 years and <=60 years old at the time of informed consent
4. Body mass index (BMI) >=18 and <30 kg/m2 at Screening

Exclusion criteria

1. Clinically significant illness or disease (e.g. psychiatric disorders, disorders of the gastrointestinal tract, liver [including Gilbert*s syndrome], kidney [including nephrectomy], respiratory system, endocrine system, haematological system, neurological system, or cardiovascular system, infection, or subjects who have a congenital abnormality in metabolism) within 8 weeks of dosing, or any clinically abnormal symptom or organ impairment, as judged by the Investigator, found by medical history, physical examinations, vital signs, electrocardiogram (ECG) finding, or either abnormal laboratory values or laboratory test results at Screening or Baseline (either Day -2 or Day -1)
2. Presence of any condition in which an opioid is contraindicated (e.g. respiratory depression, asthma, sleep apnea, ileus, etc.), unless regarded not clinically significant by the Investigator
3. Females who are breastfeeding or pregnant at Screening or Baseline (Day -2) (documented by a negative β human chorionic gonadotropin [β-hCG] or human chorionic gonadotropin [hCG] test with a minimum sensitivity of 25 IU/L or equivalent units of β-hCG [or hCG]). A negative urine pregnancy test is required before the administration of the first dose per cohort
4. Females of childbearing potential. NOTE: All females will be considered to be of childbearing potential unless they are postmenopausal (amenorrheic for at least 12 consecutive months, and without other known or suspected cause) or have been sterilized surgically (i.e. bilateral tubal ligation, total hysterectomy, or bilateral oophorectomy, all with surgery at least 6 weeks before dosing)
5. Any history of gastrointestinal surgery that may affect PK profiles of ALKS 6610 (e.g. hepatectomy, digestive organ resection) or other conditions that may

impact absorption (malabsorption syndrome, inflammatory bowel disease, etc.) at Screening
6. A prolonged QT/QTc interval (QTcF >450 ms in males, and QTcF >470 ms in females) demonstrated on ECG at Screening or Baseline (either Day -2 or Day -1). A history of risk factors for torsade de pointes (e.g. heart failure, hypokalaemia, family history of long QT Syndrome)
7. Left bundle branch block at Screening or Baseline (either Day -2 or Day -1)
8. Systolic blood pressure (BP) >140 or <90 mmHg or diastolic BP >90 or <50 mmHg at Screening or Baseline (either Day -2 or Day -1) or history of clinically relevant orthostatic hypotension
9. Heart rate less than 45 beats per minute (bpm) or more than 100 bpm at Screening or Baseline (either Day -2 or Day -1)
10. History of myocardial infarction, ischemic heart disease, or cardiac failure at Screening
11. History of clinically significant arrhythmia or uncontrolled arrhythmia as determined by the Investigator at screening
12. Subjects who have demonstrated allergic reactions (e.g. food, drug, atopic reactions or asthmatic episodes) which, in the opinion of the Investigator, interfere with their ability to participate in the trial
13. Positive Hepatitis A antibodies (HAV IgM), Hepatitis B surface antigen (HBsAg), Hepatitis B antibodies (Anti-HBc), Hepatitis C antibodies (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at Screening
14. Use of nicotine containing products within 2 weeks before the first dose of study drug (Day 1)
15. History of opioid use disorder per Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) classification, or other drug/substance or alcohol dependency or abuse before Screening, or those who have a positive drug test or alcohol test at Screening or Baseline (Day -2)
16. Use of prescription and non-prescription medications, herbal and nutritional supplements within 2 weeks prior to dosing or 5 half-lives, whichever is longer. Exceptions will only be made with approval of the Principal Investigator and Alkermes* Medical Monitor
17. Any history of lifetime suicidal ideation or behaviour, confirmed by a Columbia Suicide Severity Rating Scale (C-SSRS) response of *Yes* to questions 4 or 5 at Screening
18. Currently enrolled in another clinical study, used any investigational drug or device within 3 months prior to dosing, or having participated in more than 4 investigational drug studies within 1 year prior to Screening
19. Receipt of blood products within 4 weeks, blood donation or blood loss of >250 mL within 8 weeks, or donation of plasma within 1 week of first ALKS 6610 dose (Day 1)
20. Subject has any finding that may compromise the safety of the subject (e.g., difficulty with venous access) or affect their ability to adhere to the protocol requirements
21. Is employed by Alkermes, the Investigator or study site, (permanent, temporary contract worker, or designee responsible for the conduct of the study) or is immediate family* of an Alkermes, Investigator, or study site

employee
22. Positive SARS-CoV-2 PCR analysis prior to first dosing.
* Immediate family is defined as a spouse, parent, sibling, or child, whether biological or
legally adopted

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):	21-01-2020
Enrollment:	56
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ALKS 6610
Generic name:	NA

Ethics review

Approved WMO

Date:	16-12-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	02-01-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-06-2020
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

ID: 20667
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2019-004075-39-NL
CCMO	NL71886.056.19

Study results

Date completed:	23-10-2020
Results posted:	28-12-2021

First publication
12-10-2021

URL result

URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File