A double-blind, placebo-controlled, dose escalation study of the safety, tolerability, pharmacokinetics, and pharmacodynamics of KCP506 in healthy subjects

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The purpose of this study is to investigate how safe the new compound KCP506 is and how well it is tolerated when it is administered to healthy volunteers. It will also be investigated how quickly and to what extent KCP506 is absorbed and eliminated...

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

Summary

ID

NL-OMON55203

Source
ToetsingOnline

Brief title
SAD/MAD study investigating safety, tolerability, PK and PD of KCP506

Condition

- Other condition

Synonym
chronic pain

Health condition

Chronic pain

Research involving
Human

Sponsors and support

Primary sponsor: Kineta Chronic Pain, LLC
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: KCP506, Pharmacokinetics, Safety, Tolerability

Outcome measures

Primary outcome

• To evaluate the safety and tolerability of KCP506 in healthy adults,

following a single intravenous (iv) or subcutaneous (sc) injection at

escalating dose levels

• To evaluate the safety and tolerability of KCP506 in healthy adults,

following multiple iv or sc injections at escalating dose levels

Secondary outcome

• To evaluate the PK of KCP506 in healthy subjects, following a single iv or sc

injection at escalating dose levels

• To evaluate the PK of KCP506 in healthy subjects, following multiple iv or sc

injections at escalating dose levels

Study description

Background summary

KCP506 is a new compound that is being research as a potential treatment for chronic pain. The study compound is not registered in the Netherlands as a medication. This means that the study compound is still in development and that it is not known whether the study compound is safe and if it works. Current

treatment options for chronic pain include so-called non-steroidal-anti-inflammatory drugs (NSAIDs) and opioid-based therapeutics. Disadvantages of these treatment options are that NSAIDs are not always effective in all patients and opioids are addictive and may have unwanted effects on brain functioning. KCP506 has a different working mechanism and works by inhibiting a protein called *α9α10 nicotinic acetylcholine receptor*. This protein is important for pain perception. By inhibiting it, KCP506 aims to reduce pain sensation.

Study objective

The purpose of this study is to investigate how safe the new compound KCP506 is and how well it is tolerated when it is administered to healthy volunteers. It will also be investigated how quickly and to what extent KCP506 is absorbed and eliminated from the body (this is called pharmacokinetics). KCP506 has not been administered to humans before. It has been previously tested in the laboratory and on animals. KCP506 will be tested at various dose levels.

Study design

KCP506 or placebo will be given as either an intravenous infusion (IV; solution of the study compound that will be administered directly in a blood vessel) or as an injection / infusion under the skin (SC; subcutaneous).

Part A:
Participation from screening until the follow-up visit will last about 5 weeks.
In total, the volunteer will come to the research center 4 times:
• 1 screening visit
• 1 stay in the research center of 5 days (4 nights)
• 2 visits to the research center on Day 8 and 15

Part B:
Participation from screening until the follow-up visit will last about 7 weeks.
In total, the volunteer will come to the research center 4 times:
• 1 screening visit
• 1 stay in the research center of 17 days (16 nights)
• 2 visits to the research center on Day 20 and 27

Part C:
participation from screening until the follow-up visit will last about 13 weeks
In total, the volunteer will come to the research center 8 times:
• 1 screening visit
• 2 stays in the research center of 3 days (2 nights)
• 4 visits to the research center on Day 4 and 8

Intervention

Part A:
Group Study compound Dose* Route of administration
1 KCP506 or placebo 1.0 mg/kg In a vein
2 KCP506 or placebo 3.0 mg/kg In a vein
3 KCP506 or placebo 10 mg/kg In a vein
4 KCP506 or placebo 30 mg/kg In a vein
5 KCP506 or placebo 100 mg/kg In a vein
6 KCP506 or placebo 5.0 mg/kg Under the skin as 1 or 2 injections
7 KCP506 or placebo 50 mg/kg Under the skin as an infusion

Part B:

Group Day Study compound Dose Route of administration
8 1, 4, 7, 10, and 13 KCP506 or placebo 50 mg/kg Under the skin
9 1, 4, 7, 10, and 13 KCP506 or placebo 30 mg/kg In a vein
10 1, 4, 7, 10, and 13 KCP506 or placebo 100 mg/kg In a vein
11** TBD KCP506 or placebo TBD TBD

Part C:
Group: Study period 1 Study period 2
1 KCP506 (100mg/kg) Placebo
2 Placebo KCP506 (100mg/kg)

Study burden and risks

As KCP506 will be administered to humans for the first time in this study, side effects of KCP506 in humans have not been reported to date. However, KCP506 has been studied extensively in the laboratory and in animals.

KCP506 was found to be well tolerated in an animal study where rats were given repeat-doses of up to 1000 mg/kg KCP506. In humans, this is equal to a dose of approximately 166 mg/kg compared to rats and 333 mg/kg compared to monkeys.

Possible discomforts due to procedures
Blood sampling
Blood is drawn using an indwelling venous cannula (tube in vein in forearm). This might sometimes cause mild pain, inflammation, swelling, hardening of the vein, blood clotting and bleeding into surrounding (bruising) at the insertion site.

Part A:
In total, we will take about 120 milliliters (mL) of blood from the volunteer.
Part B:
In total, we will take about 190 milliliters (mL) of blood from the volunteer.
Part C:

In total, we will take about 100 milliliters (mL) of blood from the volunteer.

ECG
The volunteer will have small, soft pads (ECG electrodes), placed stuck temporarily on different parts of his body. There is no pain or discomfort during an ECG; however the area of skin in which the ECG pads will be stuck may need to be shaved, and the pads may cause a skin reaction such as redness or itching. Taking the pads off may cause localized irritation to the skin and/or hair loss, similar to having a plaster taken off. To monitor the volunteers heart rate (telemetry), electrodes will be pasted at specific locations on the chest and abdomen.

Coronavirus test
A sample for the coronavirus test will be taken from the back of the volunteers nose and throat using a swab. Taking the sample only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the volunteers throat may cause you him gag. When the sample is taken from the back of his nose, he may experience a stinging sensation and his eyes may become watery

Different pain tests:
Flexible plastic skewer (Von Frey).
At the start of each examination day, we gently prick the skin of the forearm with flexible plastic pricks. In this way we test what the volunteer's pain threshold is. We poke around the area where capsaicin has been applied. When the feeling of the injection changes from non-painful to painful, the volunteer indicates this. For example, we test the sensitivity of the skin. During the day we test this several times to determine the change in sensitivity (total test time: ± 3 minutes).

Pressing pain test.
During this test, through a blood pressure band an increasing pressure is exerted on the calf muscle of the volunteers right leg by means of a computer-controlled pressure regulator. In this test you will also use the electronic (*eVAS*) slider to indicate the volunteers pain threshold. By moving the slider to the right, the volunteer indicate he starts to feel pain, and by moving the slider all the way to the right the volunteer indicate that he has reached his pain threshold, whereupon the test ends and the pressure band immediately empties again. A safety maximum is set on the pressure band. The test also ends when this maximum is reached. Duration ± 3-5 minutes.

Electric pain test.
During the electrical pain test, two electrodes are placed on the skin of the shin with which electrical surges that increase in intensity are given. This determines the volunteers tolerance for pain. Connecting the electrodes to the power supply may cause a slight discharge of electricity. The pain test does not cause damage, but it does increase pain sensation. The volunteer will be

asked to use an eVAS slider to indicate his pain threshold. By sliding the slider to the right, the volunteer indicate that he starts to feel pain, and moving the slider all the way to the right indicates that the volunteer has reached his pain threshold, whereupon the electrical test is immediately terminated. It might be necessary to shave a small area of the skin on the volunteer his shin to place the electrodes. The entire procedure can cause some skin irritation that will go away within a few days. Duration ± 2 minutes.

Application of capsaicin.
Capsaicin is a composite that is also present in red and green peppers. During this study a small amount of 1% capsaicin on ethanol basis will be applied on the volunteer his forearm. 30 minutes after application of the solution we will determine if the site where the capsaicin was applied and the area around it has become more sensitive for pain stimulation. The test with flexible plastic sticks and a heat pain test will be performed to determine this. The capsaicin may cause a transient warm or burning sensation on the skin.

Heat pain test with capsaicin.
During the study period, a heat pain test is performed on both forearms. So the forearm where capsaicin has been applied, and the forearm where this has not been done. For this, a small thermal block is placed on the skin. During the test this block will gradually warm up. The volunteer will be asked to press a button the moment the heat sensation becomes painful. Thereafter, the thermal block quickly and automatically returns to a pleasant temperature. The test is performed 3 times on the capsaicin treated skin and 3 times on the healthy skin. Duration ± 5 minutes.

Cold pain test.
In this test, the volunteer first place his hand in a lukewarm water bath for 1 minute and 50 seconds. After this, the blood supply to the volunteers hand is temporarily limited before the start of the measurement by slightly inflating a blood pressure band around his arm. The volunteer will then place the same hand in a tank of ice-cold water (~1.0 °C). In this way the volunteers hand is exposed to a continuous cold stimulus for up to 2 min. This causes a pain sensation. During the measurement, the blood supply to his hand is temporarily limited by slightly inflating a blood pressure band. In this test the volunteer will also use the eVAS slider to indicate his pain threshold and moving the slider all the way to the right indicates that The volunteer has reached his pain threshold. The test ends when the time limit of 2 minutes is reached or when the volunteer indicate using the eVAS slider that the pain becomes unbearable, after which the volunteer can remove his hand directly from the cold-water bath. Duration 3-5 minutes.

Pain questionnaire.
Pain questionnaire. At the end of the pressure-, electrical-, heat and cold pain tests the volunteer will be asked to give his pain a number between 0 and 10, in which 0 means no pain at all and 10 means the worst pain he can imagine.

Additionally, the volunteer will be asked to fill in a questionnaire about how you experienced the test, e.g. was the sensation burning, stabbing, itching, etc.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Gender: male (all parts) or female (Parts A and B only)
Age: 18 to 55 years, inclusive, at screening
Weight: 50 to 105 kg, inclusive
Body mass index: 18.0 to 30.0 kg/m2, inclusive
Status: healthy subjects

Exclusion criteria

1. Previous participation in the current study.
2. Employee of PRA, CHDR or the Sponsor.
3. History of relevant drug and/or food allergies, per the Investigator*s assessment.
4. Using tobacco products within 60 days prior to first drug administration
5. History of alcohol abuse or drug addiction (including cannabis products), per the Investigator*s assessment.
6. Positive drug and/or alcohol screen (opiates, methadone, cocaine, amphetamines [including ecstasy], cannabinoids, barbiturates, benzodiazepines, tricyclic antidepressants, nicotine [cotinine - Parts A and B only]. and alcohol) at screening or first admission to the clinical research center. Tests may be repeated once at screening and once at admission in case of a suspected false positive result.
7. Average intake of more than 24 units of alcohol per week (1 unit of alcohol equals approximately 250 mL of beer, 100 mL of wine, or 35 mL of spirits).
8. Positive screen for hepatitis B surface antigen (HBsAg), antihepatitis C virus (HCV) antibodies, or antihuman immunodeficiency virus (HIV) 1 and 2 antibodies.
9. Participation in a drug study within 60 days (Parts A and B) or 90 days (Part C) or 5 drug elimination half-lives, whichever is longer) prior to the first drug administration in the current study. Participation in more than 3 other drug studies in the 10 months prior to the first drug administration in the current study.
10. Donation or loss of more than 100 mL of blood within 60 days prior to the first drug administration. Donation or loss of more than 1.5 liters of blood (for male subjects)/more than 1.0 liters of blood (for female subjects) in the 10 months prior to the first drug administration in the current study.
11. Significant and/or acute illness within 5 days prior to the first drug administration that may impact safety assessments or be consistent with COVID-19 infection, in the opinion of the Investigator.
12. Unsuitable veins for infusion or blood sampling.
13. Close contact with persons diagnosed with COVID-19 within 14 days prior to screening.
14. Positive nasopharyngeal PCR test for SARS-CoV-2 on Day -1.
15. Receipt of a vaccine within 14 days prior to the first study drug administration (Parts A and B) or either study drug administration (Part C).

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	13-10-2020
Enrollment:	108
Type:	Actual

Ethics review

Approved WMO Date:	01-07-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-08-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2020
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2021
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: 28854
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2020-002702-13-NL
CCMO	NL74314.056.20

Study results

Date completed:	14-03-2022
Results posted:	21-11-2022

First publication
21-10-2022