ISRCTN11974590 https://doi.org/10.1186/ISRCTN11974590

Phase I study, Camurus study code: HS-21-696

Submission date	Recruitment status	[X] Prospectively registered
28/04/2022	No longer recruiting	[ ] Protocol
Registration date	Overall study status	[ ] Statistical analysis plan
29/04/2022	Completed	[ ] Results
Last Edited	Condition category	[ ] Individual participant data
28/02/2025	Other	[X] Record updated in last year

Plain English summary of protocol
Background and study aims
The medicine that will be tested in this study is a compound called "CAM2038". CAM2038 is a slightly lower monthly dose of a treatment that is already marketed and prescribed in Europe called Buvidal®. Buvidal is a long-acting formulation (depot) that contains the active substance buprenorphine, which is the same active substance as is used in Subutex®. The lowest dose of Buvidal that is currently approved for once monthly treatment is 64 mg.
The Sponsor is developing a lower monthly dose of Buvidal (CAM2038) than the currently approved lowest dose to treat opioid dependence (this means heroin and morphine addiction). The main purpose of the study is to investigate how CAM2038 is taken up, metabolised (chemically broken down), distributed throughout the body and excreted from the body. The study will also see how safe CAM2038 is and how well it is tolerated after dosing. The study will compare the information from the three medicines (CAM2038, Buvidal and Subutex) with each other. As these three medications are quite strong medicines, participants will need to take naltrexone, which is a drug that blocks the effects of CAM2038, Buvidal and Subutex.

Who can participate?
Healthy women (who are not pregnant or breastfeeding) and men who are 18 to 65 years of age.

What does the study involve?
About 32 participants will take part in the study. They will be divided into four treatment groups. There will be eight participants in each of these treatment groups. The study is divided into two treatment periods with a washout period (a period to allow a medicine to be removed from the body) of 1 week in between the two periods. During the first period, participants will take daily doses of Subutex for a week. After the 1-week washout period, participants will get a single dose of either CAM2038 or Buvidal. The participants will then be followed up for 10 weeks.

What are the possible risks and benefits of participating?
Taking part in this study is not expected to provide participants with any direct medical benefit. However, the information we get from this study may help improve the treatment of opioid dependence.
The study involves some risks to the participants, but these risks are generally mild and easily monitored. People interested in taking part will be informed about the risks, as well as procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible side effects.

Participants may have unwanted effects of the drugs used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects. Participants will be told about the known unwanted effects of CAM2038, Buvidal, Subutex and naltrexone, and possible unwanted effects based on human and laboratory studies or knowledge of similar medicines.

Where is the study run from?
Parexel Early Phase Clinical Unit (UK)

When is the study starting and how long is it expected to run for?
May to September 2022

Who is funding the study?
Camurus AB (Sweden)

Who is the main contact?
Head of Medical Information Camurus, hs-21-696@camurus.com

Contact information

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Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-000393-26

Integrated Research Application System (IRAS)
1005072

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 1005072, Camurus study code: HS-21-696

Study information

Scientific Title
Phase I study, Camurus study code: HS-21-696

Study objectives
The purpose of this study is to evaluate the pharmacokinetics (PK), relative bioavailability, safety and tolerability of buprenorphine (BPN) and norbuprenorphine (norBPN) after a single administration of low-dose CAM2038, a single dose of 64 mg CAM2038 (Buvidal®), and repeated doses of sublingual buprenorphine (SL BPN; Subutex®) in healthy volunteers under naltrexone blockade.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 31/03/2022, London - Brent Research Ethics Committee (80 London Road, Skipton House, London, SE1 6LH, UK; +44 (0) 20 7104 8137; brent.rec@hra.nhs.uk), ref: 22/LO/0156
2. Approved 31/03/2022, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0) 20 3080 6000; info@mhra.gov.uk), ref: CTA 42800/0011/001-0001

The HRA has approved deferral of publication of trial details.

Study design
Phase I trial to assess safety, tolerability and pharmacokinetics in approximately 32 healthy volunteers

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
A total of 32 healthy volunteers will be randomized into one of four treatment groups in the study. In Period 1 of the study, two groups of 16 subjects each will be administered 7 repeated daily doses of 2 or 6 mg SL BPN, followed by a 7-day washout period. A single dose of either low-dose CAM2038 or 64 mg CAM2038 will then be administered subcutaneously in the buttock to 8 subjects in each subgroup, whereafter the subjects will be followed for 10 weeks (Period 2). The subjects will be under naltrexone blockade during treatment with SL BPN and CAM2038 to mitigate the anticipated adverse effects related to BPN in healthy volunteers.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
CAM2038 (buprenorphine), Buvidal® (buprenorphine), Subutex® (buprenorphine)

Primary outcome(s)
BPN and norBPN PK parameters (Cmax, tmax, AUC0-inf, and t1/2) after a single dose of low-dose CAM2038. Blood samples will be taken pre-dose and at specified time points until Day 85/End of Study

Key secondary outcome(s))
1. BPN PK parameters for single dose CAM2038 (DAUC0-inf) and for steady-state SL BPN (DAUCτ). Blood samples for SL BPN will be taken from Day 5 until 24 h after the last dose. Blood samples for CAM2038 will be taken pre-dose and at specified time points until Day 85/End of Study.
2. BPN and norBPN PK parameters (DCmax, DAUC0-last, DAUC0-inf) for single dose CAM2038. Blood samples will be taken pre-dose and at specified time points until Day 85/End of Study.
3. Adverse events, local tolerability and changes in laboratory values, vital signs and electrocardiogram parameters. Safety assessments will be performed throughout the study.

Completion date
16/09/2022

Eligibility

Key inclusion criteria
1. Voluntary and valid written informed consent to participate in the study provided before performing any study-related procedures.
2. Male or female subjects aged 18 to 65 years old (inclusive) at the time of screening.
3. Body mass index range of 18.5 to 30.0 kg/m2, inclusive, and body weight of at least 50 kg at the time of screening.
4. Willing to abstain from activities that require focused attention, e.g. driving a car or other vehicles, operating machines, or engaging in potentially dangerous activities that require focused attention and intact physical balance during the study.

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
32

Key exclusion criteria
1. Known contraindication or hypersensitivity to BPN, excipients of CAM2038, other opioids or naltrexone.
2. Clinically significant history of allergic conditions, including drug allergies, asthma (except childhood asthma), chronic eczema, or anaphylactic reactions, but excluding untreated, asymptomatic, seasonal allergies.
3. History or evidence of clinically significant cardiovascular, gastrointestinal, endocrinologic, hematologic, hepatic, immunologic, metabolic, urologic (including any obstruction to urinary flow such as prostatic hypertrophy, urinary hesitancy etc.), pulmonary, neurologic (including history of fits), dermatologic, psychiatric, or renal disease, or other major disease or malignancy, as judged by the Investigator.
4. Clinically significant laboratory test result at screening that contraindicates study participation.
5. Use of any cytochrome P450 (CYP) 3A4-modifying drugs and/or other products, including strong or moderate inhibitors of CYP enzymes (e.g. cimetidine, fluoxetine, quinidine, erythromycin, ciprofloxacin, fluconazole, ketoconazole, diltiazem, and HIV antivirals) and strong or moderate inducers of CYP enzymes (e.g. barbiturates, carbamazepine, glucocorticoids,

phenytoin, St. John´s Wort and rifampicin) within 2 weeks before the first administration of SL BPN or less than 5 half-lives of the medication, whichever is longer.
6. Positive serology test for hepatitis B surface antigen, hepatitis C virus antibodies, or antibodies to HIV type 1 (HIV-1) and/or type 2 (HIV-2) at screening.
7. Pregnant, lactating, or planning to become pregnant during the study.
8. Female subject of childbearing potential unwilling to use a highly effective method of contraception during the study.
9. Male subject unwilling to use condoms with spermicide during the study.
10. Any condition requiring regular medication, including herbal products, or predicted need of any concomitant medication during the study.
11. Heart rate of <40 beats per minute (bpm) or >90 bpm, systolic blood pressure <80 mmHg or >140 mmHg or diastolic blood pressure <40 mmHg or >90 mmHg at the screening visit.
12. QTcF >450 ms for males and >470 ms for females at the screening visit, or a history of Torsades de Pointes, or familial long QT syndrome at screening.
13. History or presence of alcohol and/or drug dependence or addiction, or positive urine drug or alcohol screen at the screening visit or at any point prior to randomization.
14. Presence of excessive alcohol consumption (regular alcohol intake >21 units per week for males and >14 units of alcohol per week for females). One unit is equal to approximately 8 g of pure alcohol (200 mL) of beer (5%), one small glass (100 mL) of wine (10%), or 25 mL of spirits (40%).
15. Smoking more than 10 cigarettes (or an equivalent amount of tobacco) per day within 3 months before screening.
16. Intake of any food or any drinks containing grapefruit, Chinese grapefruit (pomelo) or Seville orange (including marmalade) within 48 hours before the first administration of SL BPN until Day 85/End of Study.
17. Excessive use of caffeine-containing beverages exceeding 500 mg caffeine/day (5 cups of coffee) and the inability to refrain from the use of caffeine-containing beverages for 24 hours before each visit and during confinement at the Unit.
18. Intake of any medication (except paracetamol up to 2 g per day), including over-the-counter medication, herbal and dietary supplements such as St John's Wort, vitamins, and minerals that could affect the outcome of the study, within 2 weeks before the first administration of SL BPN or less than 5 half-lives of the medication, whichever is longer.
19. Veins unsuitable for venipuncture or cannulation.
20. Blood donation within 2 months before screening.
21. Participation and dosing with an experimental drug in another study within 3 months before first administration of SL BPN (calculated from last dosing of an experimental drug).
22. Is an employee of the Investigator or the study site, with direct involvement in the proposed study or other studies under the direction of the Investigator or study site or is a family member of an employee or of the Investigator.
23. Subject reports AEs prior to randomization that are considered related to naltrexone and that, in the Investigator's opinion, would inhibit compliance with naltrexone dosing during the remainder of the study.
24. Any other condition or deviation that, in the Investigator's opinion makes the subject unsuitable for participation in the study.
25. Subject has clinical signs and symptoms consistent with COVID-19, e.g. fever, dry cough, dyspnea, sore throat, fatigue, loss of taste or smell, or confirmed infection by appropriate laboratory test at screening or prior to admission on Day -1.
26. Subject has had a severe course of COVID-19 as judged by the Investigator based on medical history (e.g. extracorporeal membrane oxygenation, mechanically ventilated).
27. COVID-19 vaccination within 7 days before the first dose of SL BPN.

Date of first enrolment

03/05/2022

Date of final enrolment
23/05/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Parexel Early Phase Clinical Unit
Level 7, Northwick Park Hospital
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Sponsor information

Organisation
Camurus AB

Funder(s)

Funder type
Industry

Funder Name
Camurus AB

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No