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A Phase I, randomized, open-label, active-controlled, three-way treatment trial assessing pharmacokinetics, bioavailability and safety of three doses of CAM2038 q1w (once-weekly) (buprenorphine FluidCrystal® injection depot), versus active comparators, intravenous and sublingual buprenorphine, in healthy volunteers under naltrexone blockage

Submission date
07/02/2014

Recruitment status
No longer recruiting

Registration date
19/05/2014

Overall study status
Completed

Last Edited
12/02/2021

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Before a new medicine can be registered for use in humans, it is necessary to confirm that it is safe and effective. This is done by carrying out a research study. The medicine tested in this study is a compound called CAM2038, delivered as a once weekly injection under the skin (subcutaneous injection). Camurus AB is developing the study medication for treating addiction to opioids. This study will compare the study medication to two similar products already on the market, namely intravenous Temgesic® (administered into a vein) and Subutex® tablets, referred to as the comparator drug. The main aim of the study is to see how safe the study medication is and how well it is tolerated after it is given to participants. The study will also investigate how the study medication is taken up, metabolised (chemically broken down), distributed throughout the body and excreted.

Who can participate?
Healthy adults, male or female, between 18 and 65 years of age.

What does the study involve?
Participants will be randomly allocated to be treated with one of three doses of subcutaneous CAM2038, intravenous Temgesic® or Subutex® tablets.

What are the possible benefits and risks of participating?
There are no direct benefits of participating in this study. The results could help to improve the treatment of opioid dependence. Possible risks include overdose of buprenorphine, a reaction at the injection site, and an allergic reaction to buprenorphine or other ingredients in CAM2038.

Where is the study run from?
PAREXEL International Early Phase Clinical Unit, Harrow, UK.

When is the study starting and how long is it expected to run for?
The study started in December 2013 and will run until April 2014.

Who is funding the study?
Camurus AB (Sweden).

Who is the main contact?
Ms Tshibuabua Kabasela

Contact information

Type(s)
Scientific

Contact name
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Clinical Trials Information System (CTIS)
2013-004004-19

Protocol serial number
Protocol HS-11-426, Final Version 1.0 dated 09-Oct-2013

Study information

Scientific Title
A Phase I, randomized, open-label, active-controlled, three-way treatment trial assessing pharmacokinetics, bioavailability and safety of three doses of CAM2038 q1w (once-weekly) (buprenorphine FluidCrystal® injection depot), versus active comparators, intravenous and sublingual buprenorphine, in healthy volunteers under naltrexone blockage

Study objectives
Characterisation of the pharmacokinetic profiles, including dose proportionality and linearity and safety of buprenorphine after subcutaneous single-dose injections of CAM2038 q1w versus active comparators, intravenous and sublingual buprenorphine, respectively, in healthy volunteers under naltrexone blockage.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central - Oxford A (Bristol Research Ethics Committee Centre), 12/12 /2013, ref: 13/SC/0548

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Treatment of opioid dependence

Interventions
CAM2038 is a ready-to-use, extended release product being developed by Camurus AB for the treatment of opioid dependence. This trial will be conducted in the CRO PAREXEL Clinical Unit Early Phase, Northwick Park Hospital (Level 7), UK. The population in question are healthy adult male or female volunteers aged between ≥18 and ≤65 years. Participants will be approached by the recruitment team of the clinical research, either from our existing volunteer database (which is bolstered by advertising on a daily basis) or participants responding to advertisements. Once a volunteer is fully registered on PAREXELs database, participants are contacted to discuss the particular study via phone, text or e-mail. Potentially suitable volunteers will then be invited to information sessions held by the responsible investigator to explain study details and participation criteria. As soon as the volunteer confirms written consent, he/she will be invited for a screening visit. In case of successfully screening, eligible subjects will be randomized in a 1: 1:1 ratio to one of three parallel treatment groups (Group A, Group B or Group C). Randomization to treatment groups A, B and C will occur pre-dose of the IV buprenorphine injection on Day 1.

CAM2038 50 mg/mL q1w (Buprenorphine FluidCrystal® Injection depot) 50 mg/mL:
Group A: CAM2038 50 mg/mL q1w 8 mg buprenorphine base (0.16 mL) subcutaneous injection
Group B: CAM2038 50 mg/mL q1w 16 mg buprenorphine base (0.32 mL) subcutaneous injection
Group C: CAM2038 50 mg/mL q1w 32 mg buprenorphine base (0.64 mL) subcutaneous injection

Reference products:
Group A, B and C: IV buprenorphine (Temgesic®) 0.6 mg buprenorphine base (2.0 mL)
Group A: SL buprenorphine (Subutex®) tablets 8 mg buprenorphine base (1 tablet of 8 mg)
Group B: SL buprenorphine (Subutex®) tablets 16 mg buprenorphine base (2 tablets of 8 mg)
Group C: SL buprenorphine (Subutex®) tablets 24 mg buprenorphine base (3 tablets of 8 mg)

Pre-medication:
Oral naltrexone (Nalorex®) 50 mg film-coated tablets; initial starting dose of 100 mg on Day -1, and 50 mg daily from Day 1 to Day 39. Administration period of oral naltrexone may be extended at the discretion of the investigator.

Intervention Type
Other

Phase
Phase I

Primary outcome(s)
1. Pharmacokinetics sampling times:
1.1. Single IV buprenorphine injection on Day 1: predose (within 45 minutes) and at 5, 10, 15, 20, 30 and at 40 minutes, and at 1, 1.5, 2, 4, 6, 10 and 24 hours post dosing.
1.2. Buprenorphine: sublingual 8 mg, 16 mg or 24 mg: predose (within 45 minutes) and at 10, 20, 30 and 40 minutes and at 1, 1.5, 2, 3, 4, 6, 10 and 24 hours post dosing for the 1st dose and 7th dose, and additionally at 48 and
72 hours post dosing for the 7th dose.
1.3. CAM2038 50 mg/mL q1w 8 mg, 16 mg and 32 mg: predose (within 45 minutes) and at 0.5, 1, 2, 4, 6, 10, 24, 36 and 48 hours post dosing, subcutaneous injection: and at 3, 4, 5, 7, 14, 21 and 28 days post dose.

Key secondary outcome(s))
1. Vital signs and 12-lead ECGs:
1.1 Single IV buprenorphine injection: on Day 1: on Day -1, on Day 1 at predose (within 45 minutes) and at 30 minutes, and at 1, 2, 4, 6, 10 and 24 hours post dosing.
1.2. Buprenorphine sublingual 8 mg, 16 mg or 24 mg: predose (within 45 minutes) and at 30 minutes, and at 1, 2, 4, 6, 10 and 24 hours post dosing for the 1st dose and 7th dose, and additionally at 48 and 72 hours post dosing
for the 7th dose.
1.3. CAM2038 50 mg/mL q1w 8 mg, 16 mg and 32 mg: predose (within 45 minutes) and at 0.5, 1, 2, 4, 6, 10, 24 and 48 hours, and at the visits on post dose days 3, 4, 5, 7, 14, 21 and 28.
2. Pulse oximetry: on Day 1, Day 8, Day 14 and Day 21 continuous O2 saturation monitoring will be performed from approximately 10 minutes predose. Abnormal SpO2 values will be identified as those outside (above or below) the reference range (91-100%). Continuous SpO2 monitoring will be performed until at least 6 hours postdose for the IV buprenorphine (Temgesic) and for the SL buprenorphine (Subutex®). Continuous SpO2 monitoring will be performed until at least 36 hours postdose for the SC CAM2038 injections. SpO2 values will be recorded at the same time points as the vital signs.
3. Safety questionnaires to be completed for the single IV buprenorphine injection on Day 1, for the 1st dose and 7th dose of SL buprenorphine 8 mg, 16 mg and 24 mg and for the single subcutaneous CAM2038 50 mg/mL q1w 8 mg, 16 mg and 32 mg dose on Day 21.
4. NAS scores for dizziness, euphoria, nausea, sedation and dysphoria: predose and at 0.5, 1, 2, 4, 6, 10, and 24 hours post dosing.
5. ARCI-49: predose and at 24 hours post dosing.
6. Modified SOWS: predose, on discharge from the unit, and at follow-up.

Completion date
30/04/2014

Eligibility

Key inclusion criteria
Participants who meet the following criteria will be considered suitable to participate in the clinical study:
1. Are able to provide written informed consent to participate in the trial and able to understand the procedures and trial requirements
2. Are healthy adult male or female, ≥18 and ≤65 years of age at the time of signing of informed consent
3. Body mass index (BMI) range of 18.5 to 30.0 kg/m2, inclusive, and body mass of at least 50 kg
4. If female and of childbearing potential, is not lactating and not pregnant (has negative pregnancy test results at screening)
5. If female, is of non-childbearing potential (defined as postmenopausal for at least 1 year or surgically sterile [bilateral tubal ligation, bilateral oophorectomy, or hysterectomy]) or practicing one of the following medically acceptable methods of birth control and agrees to continue with the regimen throughout the trial:
5.1. Oral, implantable, or injectable contraceptives for 3 consecutive months before screening, in combination with a condom
5.2. Intrauterine device (IUD) in combination with a condom
5.3. Double barrier method (condoms, sponge, diaphragm, or vaginal ring with spermicidal jellies or cream)
6. Are willing and able to comply with the trial requirements and complete the trial assessments (e.g., providing urine sample under observation, completing questionnaires, abstaining 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)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Participants who meet one or more of the following criteria will not be considered eligible to participate in the clinical study:
1. Have a known contraindication or hypersensitivity to buprenorphine or other opioids.
2. Have any clinically significant history of allergic conditions (including drug allergies, asthma, eczema or anaphylactic reactions, but excluding untreated asymptomatic, seasonal allergies).
3. Have any clinically significant laboratory test result that, in the opinion of the investigator, could compromise the participant's welfare, ability to communicate with the trial staff, or

otherwise contraindicate trial participation.
4. Have any clinically significant unstable cardiac, respiratory, neurological, immunological, endocrinological, hematological, bile duct, urological or renal disease or any other condition that, in the opinion of the investigator, could compromise the participant's welfare, ability to communicate with the trial staff, or otherwise contraindicate trial participation.
5. Current use of agents metabolized through Cytochrome P450 3A4 (CYP 3A4) such as azole, antifungals (e.g. ketoconazole), macrolide antibiotics (e.g. erythromycin), or protease inhibitors (e.g. ritonavir, indinavir and saquinavir).
6. Current dependence (by DSM-IV criteria) of any psychoactive substance other than opiates, caffeine or nicotine dependence.
7. Prior or current enrolment in an opiate substitution or addiction rehabilitation program (i.e. methadone, levoalphaacetylmethadol).
8. Have tested positive for human immunodeficiency virus (HIV). Participants with hepatitis infection and no significant viral load, no acute signs of inflammation, and no clinical necessity for therapy will be allowed.
9. Are considered by the investigator, for any reason (including, but not limited to, the risks described as precautions, warnings, and contraindications in the current version of the Investigators Brochure for CAM2038 50 mg/mL q1w [buprenorphine FluidCrystal® injection depot]), to be an unsuitable candidate to receive the trial medication.
10. Have any other condition or deviation that, in the opinion of the investigator, makes the participant unsuitable for participation in the trial.
11. Is an employee of the investigator or the trial site, with direct involvement in the proposed trial or other studies under the direction of the investigator or trial site, or is a family member of an employee or of the investigator.
12. Veins unsuitable for repeat venipuncture.
13. Any condition requiring regular concomitant medication including herbal products, or predicted need of any concomitant medication during the study.
14. Intake of any medication (except paracetamol [up to 2 g per day]) including over-the-counter (OTC) medication, herbal and dietary supplements such as St Johns Wort, vitamins and minerals that could affect the outcome of the study, within 2 weeks before the first administration of the IMP or less than 5 times the half-life of that medication, whichever is the longer.
15. A pulse of <40 bpm or >90 bpm; mean systolic blood pressure (SBP) <90 mmHg or >140 mmHg; mean diastolic blood pressure (DBP) <40 mmHg or >90 mmHg (triplicate measurements, resting in supine position for at least 5 minutes; pulse measured automatically).
16. A positive orthostatic hypotension test with symptoms of orthostatic hypotension at screening or on Day -2. A positive orthostatic hypotension test defined as decreased SBP ≥20 mmHg between supine and standing and/or decrease in DBP ≥10 mmHg between supine and standing.
17. A mean corrected QT interval using Fridericias formula (QTcF) interval >450 ms (for males) and >470 ms (for females) or a history of Torsade´s de Pointes.
18. Excessive use of caffeine-containing beverages exceeding 500 mg caffeine/day (five cups of coffee) and the inability to refrain from the use of caffeine-containing beverages during confinement in the Clinical Unit.
19. History or presence of drug addiction (positive urine drug screen).
20. Excessive alcohol consumption.
21. History of smoking more than 10 cigarettes (or equivalent amount of tobacco) per day within 3 months prior to the first admission to the Clinical Unit.
22. Presence or history of alcohol abuse, as confirmed by participants general practitioner (GP).
23. 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 the investigational product and the inability to stop such intake during the study.
24. Blood donation within 3 months before the first administration of the investigational

product.
25. Participation in another study with an experimental drug within 3 months before the first administration of the investigational product.
26. Any psychological, emotional problems, any disorders or resultant therapy that is likely to invalidate informed consent, or limit the ability of the participant to comply with the protocol requirements.
27. Inability to give written informed consent or to comply fully with the protocol.
28. Have received treatment with any other IMP in the last 3 months before administration of the first dose in this clinical study.
29. Are unlikely to comply with the protocol requirements, instructions and study-related restrictions (e.g. uncooperative attitude, inability to return for visits and improbability of completing the clinical study)

Date of first enrolment
16/12/2013

Date of final enrolment
30/04/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
PAREXEL International
Harrow
United Kingdom
HA1 3UJ

Sponsor information

Organisation
Camurus AB (Sweden)

Funder(s)

Funder type
Industry

Funder Name
Camurus AB (Sweden)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2018	12/02/2021	Yes	No
HRA research summary			28/06/2023	No	No