ISRCTN24987553 https://doi.org/10.1186/ISRCTN24987553

CAM2038, pharmacokinetics (PK), bioavailability and safety in healthy volunteers

Submission date 05/06/2014	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 29/07/2014	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 13/03/2020	**Condition category** Other	[_] 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. This is done by carrying out this study. The medicine tested in this study is a compound called CAM2038. The two strengths of CAM2038 q4w (the meaning of q4w is once monthly injection) are intended to be injected once a month, while the third strength, CAM2038 q1w (the meaning of q1w is once weekly injection) is intended to be injected once a week. 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 Temgesic® and Subutex®, referred to as the comparator drugs. The main purpose 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 through the body and excreted.

Who can participate?
Healthy adult male or female volunteers aged between ≥18 and ≤65 years.

What does the study involve?
Participants are contacted to discuss the particular study via phone, text or e-mail. Potentially suitable volunteers will then be invited to information sessions to explain study details and participation criteria. As soon as the volunteer confirms willingness, he/she will be invited for a screening visit. In case of successfully screening, eligible participants will be randomly allocated to one of three parallel treatment groups and all subjects will receive a single injection of a drug buprenorphine followed by Q1D sublingual buprenorphine of strengths ranging from 8 to 32mg single injection. Lastly, two of the groups will receive two different strengths of CAM2038 q4w and the third group will receive four repeat doses of CAM2038 q1w.

What are the possible benefits and risks of participating?
This study is for research purposes only and the participants will not receive any therapeutic benefit from participating in the study. This study will only recruit healthy volunteers. CAM2038 q1w has previously been tested and no serious side effects occurred during this study. CAM2038 q4w has only been tested in animal studies and the results showed that CAM2038 q4w is considered to be safe for human use in the proposed study of this drug product. The comparator

drugs may cause some side effects. In addition, the study medication may involve risks that are currently not known.

Where is the study run from?
This study is conducted in Northwick Park Hospital, UK.

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

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

Who is the main contact?
Dr Muna Albayaty
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Contact information

Type(s)
Scientific

Contact name
Dr Muna Albayaty

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Additional identifiers

EudraCT/CTIS number
2014-000498-38

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HS-13-487

Study information

Scientific Title

A phase I, randomized, open-label, active-controlled, three-way treatment trial assessing pharmacokinetics, bioavailability and safety of two single doses of CAM2038 (Buprenorphine FluidCrystal® Injection Depot) q4w (once monthly) and four repeat doses of CAM2038 q1w (once weekly) versus active comparators, intravenous and sublingual buprenorphine, in healthy volunteers under naltrexone blockage

Acronym
CAM

Study objectives
To characterize the pharmacokinetic (PK) profiles of buprenorphine after subcutaneous single-dose injections of CAM2038 (buprenorphine FluidCrystal® injection depot q4w (once monthly), 64 mg and 128 mg, and after four repeat doses of subcutaneous injections of CAM2038 (buprenorphine FluidCrystal® injection depot) q1w (once weekly), 16 mg in healthy volunteers under naltrexone blockage.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee North East - York, 03/04/2014, ref: 14/NE/0083

Study design
Phase I randomized open-label active-controlled three-way treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Effect of CAM2038 (Buprenorphine FluidCrystal® injection depot) in healthy volunteers

Interventions
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 responsiveness on 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 to one of three parallel treatment groups CAM2038 treatment groups (Group A, B or C).

Group A: Single SC injection of CAM2038 q4w 64 mg
Group B: Single SC injection of CAM2038 q4w 128 mg
Group C: Four repeat doses of CAM2038 q1w 16 mg

Two different strengths of a drug product CAM2038 (Buprenorphine FluidCrystal® injection depot): CAM2038 q4w (the meaning of q4w is once monthly injection) and CAM2038 q1w (the meaning of q1w is once weekly injection).
Reference products: Temgesic® and Subutex®.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
CAM2038 (Buprenorphine FluidCrystal® injection depot)

Primary outcome measure
To characterize the pharmacokinetic (PK) profiles of buprenorphine after subcutaneous single-dose injections of CAM2038 (buprenorphine FluidCrystal® injection depot q4w (once monthly), 64 mg and 128 mg, and after 4 repeat doses of subcutaneous injections of CAM2038 (buprenorphine FluidCrystal® injection depot) q1w (once weekly), 16 mg in healthy volunteers under naltrexone blockage.

Secondary outcome measures
1. To assess the absolute and relative bioavailability of buprenorphine when administered as subcutaneous single-dose injections of CAM2038 q4w, 64 mg and 128 mg versus 4 repeat doses of CAM2038 q1w, 16 mg, and active comparators, intravenous and sublingual buprenorphine, in healthy volunteers under naltrexone blockage.
2. To assess safety and tolerability of buprenorphine after subcutaneous single-dose injections of CAM2038 q4w, 64 mg and 128 mg, and after 4 repeat doses of subcutaneous injections of CAM2038 q1w, 16 mg, and active comparators, intravenous and sublingual buprenorphine, in healthy volunteers under naltrexone blockage.
3. To assess and compare PK profiles of norbuprenorphine after subcutaneous single-dose injections of CAM2038 q4w, 64 mg and 128 mg, and after 4 repeat doses of subcutaneous injections of CAM2038 q1w, 16 mg, and active comparators, intravenous and sublingual buprenorphine, in healthy volunteers under naltrexone blockage.

Overall study start date
29/04/2014

Completion date
13/09/2014

Eligibility

Key inclusion criteria
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 (asthma in childhood is acceptable).
3. Body mass index (BMI) range of 18.5 to 30.0 kg/m2, inclusive, and body weight of at least 50 kg.
4. If female, is non-lactating and non-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 gels or cream).
6. Are willing and able to comply with the trial requirements and complete the trial assessments.
7. Are 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)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
57

Key exclusion criteria
1. Have a known contraindication or hypersensitivity to buprenorphine or other opioids, confirmed at screening visit.
2. Have any clinically significant history of allergic conditions (including drug allergies, asthma, eczema, or anaphylactic reactions, but excluding untreated, asymptomatic, seasonal allergies), confirmed at screening visit.
3. Have any clinically significant laboratory test result (at screening) that contraindicates trial participation.
4. Subject has any history or evidence of any clinically significant cardiovascular, gastrointestinal, endocrinology, hematologic, hepatic, immunologic, metabolic, urologic, pulmonary, neurologic, dermatologic, psychiatric, renal and/or other major disease or malignancy, as judged by the

investigator (confirmed at screening).
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) (confirmed at screening).
6. Current dependence (by DSM-IV criteria) of any psychoactive substance other than opiates or caffeine dependence (confirmed at screening).
7. Prior or current enrolment in an opiate-substitution or addiction rehabilitation program (i.e., methadone, levo-alpha-acetylmethadol) (confirmed at screening).
8. Subject has a positive serology test for hepatitis B surface antigen, hepatitis C virus antibodies, or antibodies to human immunodeficiency virus type 1 (HIV-1) and/or type 2 (HIV-2) at screening.
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 q1w and CAM2038 q4w [buprenorphine FluidCrystal® injection depot]), to be an unsuitable candidate to receive the trial medication (confirmed at screening).
10. Have any other condition or deviation that, in the Investigators opinion, makes the subject unsuitable for participation in the trial (confirmed at screening).
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 (confirmed at screening).
12. Veins unsuitable for venipuncture.
13. Any condition requiring regular concomitant medication including herbal products, or predicted need of any concomitant medication during the study (confirmed at screening).
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. Subject has a pulse of < 40 bpm or > 90 bpm; mean SBP < 90 mmHg or > 140 mmHg; mean DBP < 40 mmHg or > 90 mmHg (measurements taken in triplicate at screening after subject has been resting in supine position for at least 5 minutes; pulse will be measured automatically).
16. Subject has orthostatic hypotension test combined with symptoms of orthostatic hypotension at Screening. Orthostatic hypotension is defined as a decrease in systolic blood pressure (SBP) ≥ 20 mmHg between supine and standing posture and/or a decrease in diastolic blood pressure (DBP) ≥ 10 mmHg combined with clinical symptoms between supine and standing.
17. Corrected QT interval using Fridericias formula (QTcF) interval > 450 ms (for males) and > 470 ms (for females) or a history or Torsade's de Pointes.
18.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 during confinement in the Clinical Unit.
19. History or presence of drug abuse or addiction (positive urine drug screen).
20. Excessive alcohol consumption (regular alcohol intake > 21 units per week for males and > 14 units of alcohol per week for females) (1 unit is equal to approximately ½ pint [200 mL] of beer, one small glass [100 mL] of wine, or one measure [25 mL] of spirits). Use of alcohol 48 hours before any study visit.
21. History of smoking more than 10 cigarettes (or equivalent amount of tobacco) per day within 3 months prior to screening.
22. 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.
23. Blood donation within 3 months prior to screening.

24. Participation and dosing with an experimental drug in another study within 3 months prior to screening.

Date of first enrolment
29/04/2014

Date of final enrolment
13/09/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
PAREXEL Early Phase Clinical Unit
London
United Kingdom
HA1 3UJ

Sponsor information

Organisation
Camurus AB (Sweden)

Sponsor details
Ideon Science Park
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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Camurus AB (Sweden)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	01/02/2017		Yes	No
HRA research summary			28/06/2023	No	No