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A study to evaluate if CD388 can prevent infection with flu virus and to assess the safety, tolerability, absorption, distribution and excretion of CD388 in healthy adults

Submission date
20/09/2022

Recruitment status
No longer recruiting

Registration date
04/04/2023

Overall study status
Completed

Last Edited
03/12/2024

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
The purpose of this research is to test the effects of an experimental drug called CD388 that may be useful in preventing infection in people infected with the Influenza virus. Influenza virus causes an infectious disease commonly referred to as 'the flu'. The Influenza virus can spread easily through the air, often by coughs and sneezes. The disease is often mild in children and most healthy people but can be severe in pregnant women, people older than 65 years, people whose immune system is down, and people with chronic conditions like diabetes, asthma or heart failure. CD388 works by stopping the growth and spread of the Influenza virus in the body. The approved treatments for the flu are drugs called zanamivir and oseltamivir, but new drugs are needed because the flu virus may be becoming 'resistant' to these drugs.

Who can participate?
Healthy adults aged 18-55 years

What does the study involve?
The study will consist of three stages: Screening, Quarantine and Follow-Up. The study will consist of two groups, which will be subdivided into smaller groups. Participants in each subgroup will receive different dose levels of CD388 or placebo but will not exceed the maximum study dose of 150 mg. The participants who are randomly assigned to receive a placebo will receive an injection under the skin in the same volume as the study drug. The participants will enter quarantine on day -6 and will be dosed with CD388 or a placebo between Day -6 and Day -2. On Day 0 the participants will be inoculated with the influenza virus. After completion of the Quarantine phase, participants will need to return to the clinic five times on Day 17, Day 28, Day 60, Day 120 and Day 180 to undergo tests.

What are the possible benefits and risks of participating?
Clinical experience of CD388 is ongoing, however, the study drug was tested in animals. In studies with rats and monkeys CD388 had no significant effect on body weight, food

consumption, heart activity, blood tests, urine tests, respiration, eye tests and other clinical tests conducted on the animals.
Risks relating to the administration procedure of CD388 include pain at the site of administration, bruising at the site, and introduction of infection. Participants will be closely monitored by clinical staff for any AEs after dosing and throughout the study as per the Schedule of Events (SoE). Administration will only be carried out by trained professionals with a thorough cleaning of the area beforehand with alcohol wipes and the use of aseptic technique throughout.
Given that the placebo is a pharmacologically inert material, there should be no risk in relation to the product being administered. Similar risks apply to the procedure of administration: pain, bruising, introduction of infection into the skin. Administration will only be carried out by trained professionals with a thorough cleaning of the area beforehand with alcohol wipes and the use of aseptic technique throughout. The risk to pregnancy and birth control is unknown. Female participants of childbearing potential must use one form of highly effective contraception. Use of hormonal contraception should start at least 2weeks before the first study visit. The contraception use must continue until 3 months or 5 effective half-lives after the last dose of the investigational medicinal product (IMP), whichever is longer. Females who are pregnant or have been pregnant within 6 months prior to the study, and females who are breastfeeding, will be excluded from the study.
Male participants must agree to use contraception from entry into quarantine and continuing until 3 months or 5 effective half-lives after the last dose of IMP, whichever is longer. They must also agree not to donate sperm following discharge from quarantine until 120 days or 5 effective half-lives after the last dose of IMP, whichever is longer.
Blood sampling may cause pain, and bruising at the site where blood is withdrawn. Participants may faint following or before the blood draw. Blood tests performed to address the health of participants at screening and during the study may indicate that a participant has an infection that he/she/they were not previously aware of. The hVIVO doctor will provide the participant's general practitioner (GP), or doctor with a referral letter if the participant agrees. Nasal sampling may cause discomfort, sneezing, watery eyes, irritated nose or nose bleeding. Sample collection will be performed by appropriately qualified and trained study staff. Participants have a 60% to 75% chance of becoming infected with the influenza virus. Typical influenza illness: abrupt onset of rhinitis, nasal stuffiness, fever, malaise, myalgia (muscle aches), and sore throat. Severe complications are not expected as these tend to occur almost exclusively in infants, elderly, and persons of any age with chronic comorbidities and significant immune compromise and not in healthy adults with no comorbidities of coinfections. The safety profile of the influenza virus is well characterised in healthy adults as this has been used for over 20 years by hVIVO. At hVIVO more than 350 healthy participants aged 18 to 64 years have been challenged with influenza H3N2 A/Perth/16/2009 virus.
Influenza infection in healthy adults usually resolves without treatment within 3 to 5 days after symptoms onset.
Strict inclusion and exclusion criteria will apply to ensure only healthy adults are enrolled in this study. There will be daily medical monitoring in a quarantine unit for at least 8 days post-HVC. Qualified medical/nursing staff will monitor for and manage any symptoms.
Influenza presence in nasal secretions can cause infection in close contacts. The duration of the quarantine has been designed to allow for the resolution of infectious virus (culturable) before discharge. This is based on experience to date with more than 350 inoculations. As appropriate, the principal investigator (PI)/delegate may request additional testing of nasal swab samples using a qualitative virus antigen test/PCR to assist in determining participants' suitability for departure. As an additional precaution, participants will be instructed to avoid close contact with vulnerable individuals for 2 weeks after they leave the quarantine unit. If a participant ever had a herpes infection (e.g., cold sores, genital herpes, or shingles), there is a small possibility infection could return after the challenge. Participants will be instructed to inform the study staff if they

currently have an active herpes infection or have had one during the 30 days before enrolment. If participants develop a cold sore, herpes or shingles may be treated.

Where is the study run from?
hVIVO Limited Services (UK)

When is the study starting and how long is it expected to run for?
June 2022 to July 2023

Who is funding the study?
Cidara Therapeutics (USA)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
1005986

Protocol serial number
CD388.SQ.2.02

Study information

Scientific Title
A proof-of-concept, randomised, double-blind, placebo-controlled, Phase IIa study to assess the prophylactic antiviral activity against influenza, safety, tolerability, and pharmacokinetics of CD388 via a human viral challenge model

Study objectives
Primary objective:
To evaluate the prophylactic efficacy of CD388 in terms of reduction of area under the viral load-time curve (VL AUC) (total amount of virus release over the time of infection) after influenza viral challenge when compared to placebo.

Secondary objective:
1. To evaluate the effect of CD388 compared to placebo, in reducing or shortening viral shedding (cells release infectious virus particles into the body) after administration of the influenza challenge virus.
2. To evaluate the effect of CD388 compared to placebo, in reducing or shortening culturable /replicating virus after administration of the influenza viral challenge.
3. To evaluate the effect of CD388 compared to placebo, in reducing clinical symptoms due to administration of influenza viral challenge.
4. To evaluate the effect of CD388 compared to placebo, in reducing the incidence of influenza infection due to administration of influenza viral challenge.
5. To evaluate the safety of CD388 when compared to placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/08/2022, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2920 230 457; Wales.REC2@wales.nhs.uk), ref: 22/WA/0191

Primary study design

Interventional

Study design
Double-blind randomized placebo-controlled trial

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Influenza

Interventions
Placebo Comparator: Placebo (Arm 1): In Cohort 1, up to 30 participants will be randomized to receive a single dose of placebo, administered by subcutaneous (SQ) injection, prior to being inoculated with the influenza challenge virus. Based on an interim analysis to be performed on data collected from the evaluation of Cohort 1 participants through the inpatient phase of the study, additional participants (of a number to be informed by the interim analysis) may be randomized into Cohort 2 in an extension of this Arm 1, to receive a single dose of placebo by SQ injection prior to viral challenge.

Experimental: CD388 High Dose (Arm 2). In Cohort 1, Up to 30 participants will be randomized to receive a single dose of 150 milligrams (mg) CD388, administered by SQ injection, prior to being inoculated with the influenza challenge virus. Based on an interim analysis to be performed on data collected from the evaluation of Cohort 1 participants through the inpatient phase of the study, additional participants (of a number to be informed by the interim analysis) may be randomized into Cohort 2 in an extension of this Arm 2, to receive a single dose of 150 mg CD388 by SQ injection prior to viral challenge.

Experimental: CD388 Low Dose 1 (Arm 3) In Cohort 1, up to 30 participants will be randomized to receive a single dose of CD388 lower than 150 mg (to be determined [TBD] based on pharmacokinetic [PK] results obtained in the first-in-human study CD388.IM.SQ.1.01), administered by SQ injection, prior to being inoculated with the influenza challenge virus. Based on an interim analysis to be performed on data collected from the evaluation of Cohort 1 participants through the inpatient phase of the study, additional participants (of a number to be informed by the interim analysis) may be randomized into Cohort 2 in an extension of this Arm 3, to receive a single dose of CD388 at the same dose level used in Arm 3 Cohort 1 participants, administered by SQ injection prior to viral challenge.

Experimental: CD388 Low Dose 2 (Optional Arm 4). Based on an interim analysis to be performed on data collected from the evaluation of Cohort 1 participants through the inpatient phase of the study, participants (of a number to be informed by the interim analysis) may be randomized into Cohort 2 in this Optional Arm 4, to receive a single dose of CD388 lower than 150 mg (TBD based on PK results obtained in the first-in-human study CD388.IM.SQ.1.01, as well as the interim analysis), administered by SQ injection, prior to being inoculated with the influenza challenge virus.

Experimental: CD388 Low Dose 3 (Optional Arm 5): Based on an interim analysis to be performed on data collected from the evaluation of Cohort 1 participants through the inpatient phase of the study, participants (of a number to be informed by the interim analysis) may be randomized into Cohort 2 in this Optional Arm 5, to receive a single dose of CD388 lower than 150 mg (TBD based on PK results obtained in the first-in-human study CD388.IM.SQ.1.01, as well

as the interim analysis), administered by SQ injection, prior to being inoculated with the influenza challenge virus

Experimental: CD388 Low Dose 4 (Optional Arm 6): Based on an interim analysis to be performed on data collected from the evaluation of Cohort 1 participants through the inpatient phase of the study, participants (of a number to be informed by the interim analysis) may be randomized into Cohort 2 in this Optional Arm 6, to receive a single dose of CD388 lower than 150 mg (TBD based on PK results obtained in the first-in-human study CD388.IM.SQ.1.01, as well as the interim analysis), administered by SQ injection, prior to being inoculated with the influenza challenge virus.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
CD388

Primary outcome(s)
VL AUC of influenza challenge virus as determined by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) on nasal samples starting a day post viral challenge (Day 1, pm) up to Day 8 (am)

Key secondary outcome(s)
1. Peak viral load of influenza as defined by the maximum viral load determined by quantifiable qRT-PCR measurements in nasal samples from Day 1 (pm) up to Day 8 (am)
2. Time (hours) to confirmed negative test by quantifiable qRT-PCR measurements in nasal samples from Day 1 (pm) to first confirmed undetectable assessment after peak measure
3. VL AUC of influenza challenge virus as determined by viral culture on nasal samples, from Day 1 (pm) up to Day 8 (am).
4. Peak viral load of influenza as defined by the maximum viral load determined by quantitative viral culture measurements in nasal samples from Day 1 (pm) up to Day 8 (am).
5. Time (hours) to confirmed negative test by quantifiable viral culture measurements in nasal samples from Day 1 (pm) to first confirmed undetectable assessment after peak measure.
6. Area under the curve over time of total clinical symptoms score (TSS-AUC) as measured by graded symptom scoring system collected three times daily from Day 1 (am) up to Day 8 (am).
7. Peak symptoms diary card score: peak of total clinical symptoms (TSS) as measured by graded symptom scoring system collected three times daily from Day 1 (am) up to Day 8 (am).
8. Peak daily symptom score: individual maximum daily sum of symptom score measured by graded symptom scoring system (participant completed symptom diary card) collected three times daily from Day 1 up to Day 8.
9. Time to symptom resolution as measured by graded daily symptom score system from the time of peak daily symptom score to time of returning to baseline score
10. RT-PCR-confirmed influenza infection, defined as two quantifiable (≥lower limit of quantification [LLOQ]) qRT-PCR measurements (reported on two or more independent samples over 2 days), from Day 1 (pm) up to Day 8 (am).
11. Occurrence of at least one positive quantitative (≥LLOQ) cell culture measurement in nasal samples, from Day 1 (pm) up to Day 8 (am).
12. RT-PCR-confirmed symptomatic influenza infection, defined as RT-PCR-confirmed influenza

infection (two quantifiable [≥LLOQ] qRT-PCR measurements [reported on two or more independent samples over 2 days]), from Day 1 (pm) up to Day 8 (am), AND TSS score ≥2 at any single timepoint (i.e., any individual symptom diary card for which the sum of symptom scores is ≥2; e.g., at a minimum, ≥1 symptom of grade ≥2, or ≥2 symptoms of grade ≥1), as measured by graded symptom scoring system (participant completed symptom diary card) collected three times daily
13. RT-PCR-confirmed moderately severe symptomatic influenza infection, defined as: RT-PCR-confirmed influenza infection (two quantifiable [≥LLOQ] qRT-PCR measurements [reported on two or more independent samples over 2 days]), from Day 1 (pm) up to Day 8 (am), AND one or more symptoms of grade ≥2 at a single timepoint (i.e., on any individual symptom card), as measured by graded symptom scoring system (participant completed symptom diary card) collected three times daily
14. Culture lab-confirmed symptomatic influenza infection, defined as: lab-confirmed culturable influenza infection (one quantifiable [≥LLOQ] cell culture measurement), from Day 1 (pm) up to Day 8 (am), AND TSS score ≥2 at any single timepoint (i.e., any individual symptom diary card for which the sum of symptom scores is ≥2; e.g., at a minimum, ≥1 symptom of grade ≥2, or ≥2 symptoms of grade ≥1), as measured by graded symptom scoring system (participant completed symptom diary card) collected three times daily
15. Occurrence of solicited adverse events (AEs) recorded from the time of SQ dosing up to the time of inoculation with the influenza challenge virus
16. Occurrence of unsolicited AEs recorded from the time of SQ dosing up to the time of the Day 28 follow-up visit
17. Occurrence of unsolicited AEs recorded from the time of SQ dosing up to the time of the Day 180 final follow-up visit

Completion date
17/07/2023

Eligibility

Key inclusion criteria
1. Written informed consent signed and dated by the participant and the PI/investigator obtained before any assessment is performed
2. Adult male or female aged between 18 and 55 years old, inclusive, on the day prior to signing the consent form
3. A total body weight ≥50 kg and body mass index (BMI) ≥18 kg/m² and ≤35kg/m²
4. In good health with no history, or current evidence, of clinically significant medical conditions, and no clinically significant test abnormalities that will interfere with participant safety, as defined by medical history, physical examination, (including vital signs), electrocardiogram (ECG), and routine laboratory tests as determined by the PI/investigator
5. Participants will have a documented medical history either prior to entering the study or following medical history review with the study physician at screening
6. The following criteria are applicable to female participants participating in the study
6.1. Females of childbearing potential must have a negative pregnancy test prior to enrolment
6.2. Females of non-childbearing potential:
6.2.1. Postmenopausal females defined as amenorrhea for ≥12 months with no alternative medical cause. A high follicle-stimulating hormone (FSH) level, within appropriate postmenopausal range, may be used to confirm postmenopausal state in the absence of combined hormonal contraception or hormone replacement therapy. If there is <12 months of amenorrhea 2 FSH samples are required at least 4 to 6 weeks apart.
6.2.2. Documented status as being surgically sterile (e.g., tubal ligation, hysterectomy, bilateral

salpingectomy, and bilateral oophorectomy)
7. The following criteria apply to female and male participants:
Female participants of childbearing potential must use one form of highly effective contraception. Hormonal methods must be in place for at least 2 weeks prior to the first study visit. The contraception use must continue until 3 months or 5 effective half-lives after the last dose of IMP, whichever is longer. Highly effective contraception is as described as the established use of hormonal methods of contraception described below (for a minimum of 30 days prior to the first study visit). When hormonal methods of contraception are used, male partners are required to use a condom with a spermicide:
7.1. Combined (oestrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation:
7.1.1. Oral
7.1.2. Intravaginal
7.1.3. Transdermal
7.2. Progestogen-only hormonal contraception associated with inhibition of ovulation:
7.2.1. Oral
7.2.2. Injectable
7.2.3. Implantable
7.3. Intrauterine device
7.4. Intrauterine hormone-releasing system
7.5. Bilateral tubal ligation
7.6. Male sterilisation (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate) where the vasectomised male is the sole partner for that woman.
7.7. True abstinence – sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant. Male participants must agree to the contraceptive requirements below at entry to quarantine and continue until 3 months or 5 effective half-lives after the last dose of IMP, whichever is longer.
7.8. Use a condom with a spermicide to prevent pregnancy in a female partner or to prevent exposure of any partner (male or female) to the IMP.
7.9. Male sterilisation with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate (please note that the use of condoms with spermicide will still be required to prevent partner exposure). This applies only to males participating in the study.
7.10. In addition, for female partners of childbearing potential, that partner must use another form of contraception such as one of the highly effective methods mentioned above for female participants.
7.11. True abstinence – sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant. In addition to the contraceptive requirements above, male participants must agree not to donate sperm following discharge from quarantine until 120 days or 5 effective half-lives after the last dose of IMP, whichever is longer.
8. Sero-suitable for the challenge virus

For further details on sero-suitability inclusion criteria, please refer to the study protocol.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
59

Key exclusion criteria
1. History of, or currently active, symptoms or signs suggestive of upper respiratory tract (URT) or lower respiratory tract (LRT) infection within 4 weeks prior to the first study visit
2. Any history or evidence of any clinically significant or currently active cardiovascular, respiratory, dermatological, gastrointestinal, endocrinological, haematological, hepatic, immunological (including immunosuppression), metabolic, urological, renal, neurological, or psychiatric disease and/or other major disease that, in the opinion of the PI/investigator may interfere with a participant completing the study and necessary investigations. For the full list of conditions please refer to the study protocol.
3. Any participants who have smoked ≥10 pack years at any time (10 pack years is equivalent to 1 pack of 20 cigarettes a day for 10 years)
4. Females who:
4.1. Are breastfeeding, or
4.2. Have been pregnant within 6 months prior to the study, or
4.3. Have a positive pregnancy test at any point during screening or prior to dosing with IMP
5. Lifetime history of anaphylaxis and/or a history of severe allergic reaction or significant intolerance to any food or drug in the last 12 months, as assessed by the PI.
6. Venous access deemed inadequate for the phlebotomy and cannulation demands of the study
7.1. Any significant abnormality altering the anatomy of the nose in a substantial way or nasopharynx that may interfere with the aims of the study and, in particular, any of the nasal assessments or viral challenge (historical nasal polyps can be included, but large nasal polyps causing current and significant symptoms and/or requiring regular treatments in the last month will be excluded)
7.2. Any clinically significant history of epistaxis (large nosebleeds) within the last 3 months of the first study visit and/or history of being hospitalised due to epistaxis on any previous occasion
7.3. Any nasal or sinus surgery within 3 months of the first study visit
8.1. Evidence of vaccinations within the 4 weeks prior to the planned date of dosing with IMP
8.2. Intention to receive any vaccination(s) before the last day of follow-up (with the exception of vaccinations recommended for COVID-19 as defined by Medicines and Healthcare products Regulatory Agency (MHRA)/government vaccination guidelines)
8.3. No travel restrictions apply after the Day 28 [±3 days] follow-up visit; however, we expect participants to be available to attend the clinic at the Day 60, Day 120, and Day 180 follow-up visits
8.4. Receipt of influenza vaccine in the last 6 months prior to the planned date of viral challenge
9. Receipt of blood or blood products, or loss (including blood donations) of 550 mL or more of blood during the 3 months prior to the planned dosing with IMP or planned during the 3 months after the final visit

10.1. Receipt of any investigational drug within 3 months prior to the planned date of dosing with IMP
10.2. Receipt of 3 or more investigational drugs within the previous 12 months prior to the planned date of dosing with IMP
10.3. Prior inoculation with a virus from the same virus family as the challenge virus
10.4. Prior participation in another HVC study with a respiratory virus in the preceding 3 months, taken from the date of viral challenge in the previous study to the date of expected viral challenge in this study
11. Use or anticipated use during the conduct of the study of concomitant medications (prescription and/or non-prescription), including vitamins or herbal and dietary supplements within the specified windows, unless in the opinion of the study physician/PI, the medication will not interfere with the study procedures or compromise participant safety. For specific exclusion please refer to study protocol.
12.1. Confirmed positive test for drugs of misuse and cotinine on first study visit. One repeat test is allowed at PI discretion.
12.2. Recent history or presence of alcohol addiction, or excessive use of alcohol (weekly intake in excess of 28 units alcohol; 1 unit being a half glass of beer, a small glass of wine, or a measure of spirits), or excessive consumption of xanthine-containing substances (e.g., daily intake in excess of 5 cups of caffeinated drinks, e.g., coffee, tea, cola)
13. A forced expiratory volume in 1 second (FEV1) <80%
14. Positive HIV, hepatitis B virus (HBV), or hepatitis C virus (HCV) test (HIV positive – via 3 confirmatory tests – Vidas, Genenius, and Determine, HBV confirmed via HbsAG, anti-HBs, and anti-HBc [IgG/IgM], and HCV confirmed via hepatitis C viral load)
15. Presence of fever, defined as participant presenting with a temperature reading of ≥37.9°C on Day -6 and/or pre-dose on Day -5
16. Those employed or immediate relatives of those employed at hVIVO or the sponsor
17. Any other finding that, in the opinion of the PI/investigator, deems the participant unsuitable for the study

Date of first enrolment
29/08/2022

Date of final enrolment
05/01/2023

Locations

Countries of recruitment
United Kingdom

Study participating centre
Not provided at time of registration
United Kingdom
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Sponsor information

Organisation
hVIVO Limited Services

Funder(s)

Funder type
Industry

Funder Name
Cidara Therapeutics

Alternative Name(s)
Cidara

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		19/09/2024	03/12/2024	No	No
HRA research summary			26/07/2023	No	No