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Evaluation of safety, tolerability, and pharmacokinetics of CCX168 in healthy subjects

Submission date 10/05/2016	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 11/05/2016	**Overall study status** Completed	
Last Edited 14/06/2023	**Condition category** Signs and Symptoms	

Plain English summary of protocol

Background and study aims:
The complement system (part of the immune system that enhances the ability of the immune system to fight infection) plays a central role in generating natural immune responses to infectious agents, foreign antigens, and tumor cells. Inappropriate or excessive activation of the complement system can lead to severe inflammation (swelling) and tissue destruction. Because of this, the complement 5a receptor has been an attractive therapeutic target for many autoimmune and inflammatory disorders (disorders in which the body's immune system attacks the body's own healthy tissue). CCX168 is a drug which acts on the complement 5a receptor, and has potential in the treatment of patients with these diseases. The aim of this study is to test the safety and tolerability of CCX168 in healthy people, and to look into the way the drug moves through the body (pharmacokinetics) and the way it works (pharmacodynamic).

Who can participate?
Healthy adults aged 19 to 45 years old

What does the study involve?
All potential participants will undergo a screening process during which blood and urine samples will be taken, medical and medication history will be obtained, and a physical examination will be performed. If eligible, the participant is enrolled and will take part in two study periods. In the first period, a single dose of either the active drug (CCX168) or a matching placebo (dummy pill) is given and participants are followed for one week during which blood and urine samples are taken, vital signs and an ECG (heart rate scan) are recorded, and physical examinations are performed daily. In the second period, multiple once or twice daily doses of either the active drug (CCX168) or a matching placebo are given for seven days and participants are followed for another week during which blood and urine samples are taken, vital signs and an ECG (heart rate scan) are recorded, and physical examinations are performed daily. Participants are discharged from the study at 4 weeks after a follow up telephone call.

What are the possible benefits and risks of participating?
Since this study mainly looks at the safety and tolerability of CCX168, there is likely to be no benefit for participants, other than the knowledge that they are potentially helping to improve understanding of how to use the medication in future studies. Safety risk is considered to be low

because CCX168 has been tested safely in lab-based studies at much higher doses than will be given in this study.

Where is the study run from?
Covance Clinical Research Unit AG (Switzerland)

When is the study starting and how long is it expected to run for?
April 2009 to September 2010

Who is the main contact?
Dr Pirow Bekker
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CL001_168

Study information

Scientific Title
A double-blind, placebo-controlled, single and multiple ascending dose phase I study to evaluate the safety, tolerability, and pharmacokinetics of CCX168 in healthy male and female subjects

Study objectives
Single and multiple oral doses of CCX168 are safe for and tolerable to healthy subjects over a range of dose levels.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the Two Basels (ECTB), 14/12/2009

Study design
Single-center double-blind placebo-controlled single and multiple dose escalation study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

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

Health condition(s) or problem(s) studied
CCX168 tolerability

Interventions
Participants are randomly allocated to one of five cohorts, which in turn are randomised to receive a different dosage of CCX168 or a placebo. Each cohort undergoes two study periods: a single dose and multiple dose phases.

Cohort 1:
Intervention group: Participants receive a single 1 mg dose CCX168 in period one and 1 mg CCX168 once daily for 7 days in period two.
Control group: Participants receive a a single dose of placebo in period one and a placebo once daily in period two.

Cohort 2:
Intervention group: Participants receive a single 3 mg dose CCX168 in period one and 3 mg CCX168 once daily for 7 days in period two.
Control group: Participants receive a a single dose of placebo in period one and a placebo once daily in period two.

Cohort 3:
Intervention group: Participants receive a single 10 mg dose CCX168 in period one and 10 mg CCX168 once daily for 7 days in period two.
Control group: Participants receive a a single dose of placebo in period one and a placebo once daily in period two.

Cohort 4:
Intervention group: Participants receive a single 30 mg dose CCX168 in period one and 30 mg CCX168 once daily for 7 days in period two.
Control group: Participants receive a a single dose of placebo in period one and a placebo once daily in period two.

Cohort 5:
Intervention group: Participants receive a single 100 mg dose CCX168 in period one and 50 mg CCX168 once daily for 7 days in period two.
Control group: Participants receive a a single dose of placebo in period one and a placebo once daily in period two.

Participants are followed for 7 days after the single dose in Period 1 and for 21 days after the 7-day dosing period in Period 2. During these follow-up periods, subjects are monitored for any safety events and blood samples are taken for PK and safety laboratory assessments.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase I

Drug/device/biological/vaccine name(s)
CCX168

Primary outcome measure
Safety and tolerability of CCX168 as measured by the incidence of adverse events and changes in safety laboratory measurements on Days 2, 3, 4, and 8 in Period 1, and Days 2 through 10, 15 and 29 in Period 2.

Secondary outcome measures
1. Pharmacokinetic profile of single and multiple oral doses of CCX168 using high-performance liquid chromatography-tandem mass spectrometry on Days 1 through 4 and Day 8 in Period 1, and Days 2 through 10 and Day 15 in Period 2.
2. The relationship between CCX168 plasma concentrations and complement 5a receptor (C5aR)-dependent CD11b upregulation in circulating neutrophils, and the relationship between CCX168 plasma concentrations and C5aR-dependent cell migration in a whole blood migration assay on Day 1 of Period 1 and Day 7 of Period 2

Overall study start date
01/04/2009

Completion date
29/09/2010

Eligibility

Key inclusion criteria
1. Male or female subjects, aged 19-45 years inclusive, who are in generally good health, whose body mass index is 19 to 29 kg/m^2
2. Willing and able to give written Informed Consent and to comply with the requirements of the study protocol
3. Negative result of the human immunodeficiency virus (HIV) screen, the hepatitis B screen, and the hepatitis C screen
4. Judged to be healthy by the Investigator, based on medical history, physical examination (including electrocardiogram [ECG]), and clinical laboratory assessments. Subjects with clinical laboratory values that are outside of normal limits and/or with other abnormal clinical findings that are judged by the Investigator not to be of clinical significance may be entered into the study.
5. Female subjects of childbearing potential, and male subjects with partners of childbearing potential, may participate if adequate contraception is used during, and for at least the four weeks after, any administration of study medication

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
19 Years

Upper age limit
45 Years

Sex
Both

Target number of participants
40 targeted

Key exclusion criteria
1. Women who are pregnant, breastfeeding, or have a positive serum pregnancy test at Screening and/or on Study Day -1
2. Expected requirement for use of any medication (with the exception of continuing use by female subjects of hormonal contraceptives in accordance with a regimen that has been stable for at least the three months prior to Screening) during the study period
3. History within the three months prior to study entry of use of tobacco and/or nicotine-containing products
4. History within one year prior to study entry of illicit drug use
5. History of alcohol abuse at any time in the past
6. History of any form of cancer
7. Consumed alcoholic beverages, or any food or drink containing grapefruit or grapefruit juice within 24 hours of screening
8. History or presence of any medical condition or disease which, in the opinion of the Investigator, may place the subject at unacceptable risk for study participation
9. Donated or lost more than 350 mL of blood or blood products within 56 days prior to screening, or donated plasma within 7 days of randomization

10. Subject's hemoglobin less than 12 g/dL (or less than 7.45 mmol/L)
11. Participated in any clinical study of an investigational product within 30 days prior to randomization
12. Subject has any evidence of hepatic disease; AST, ALT, GGT, alkaline phosphatase, or bilirubin > 1.5 x the upper limit of normal
13. Subject has any evidence of renal impairment; serum creatinine > 1.5 x upper limit of normal
14. Subject's urine tested positive at Screening and/or on Study Day -1 for any of the following: opioids, amphetamines, cannabinoids, benzodiazepines, barbiturates, cocaine, cotinine, or alcohol (Breathalyzer test allowed for alcohol)

Date of first enrolment
21/12/2009

Date of final enrolment
25/08/2010

Locations

Countries of recruitment
Switzerland

Study participating centre
Covance Clinical Research Unit (CRU) AG
Lettenweg 118
Allschwil
Switzerland
CH-4123

Sponsor information

Organisation
ChemoCentryx, Inc.

Sponsor details
850 Maude Avenue
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Sponsor type
Industry

ROR
https://ror.org/04gp12571

Funder(s)

Funder type
Industry

Funder Name
ChemoCentryx, Inc.

Results and Publications

Publication and dissemination plan
Planned publication of study results in a peer-reviewed journal.

Intention to publish date
31/12/2016

Individual participant data (IPD) sharing plan

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?
Results article	results	21/10/2016		Yes	No
Protocol file	protocol	05/10/2009	14/06/2023	No	No