A Double-Blind, Placebo-Controlled, Single and Multiple Ascending Dose Phase 1 Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of CCX872-B in Healthy Male and Female Subjects

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Primair:To evaluate the safety and tolerability of single and multiple oral doses of CCX872-B, over a range of dose levels, in healthy male and female subjectsSecundair:To evaluate the following:- Single and multiple dose pharmacokinetic profile of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON37040

Source
ToetsingOnline

Brief title
CCX872-B SAD/MAD study

Condition

- Nephropathies

Synonym
Nephropathy, nierfalen

Research involving

Human

Sponsors and support

Primary sponsor: Chemocentryx
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: CCX872-B, Diabetic nephropathy, Multiple dose, Single dose

Outcome measures

Primary outcome

Pharmacodynamics:

- Plasma levels of MCP-1 and possibly MCP-2, 3, 4 and other chemokines and

cytokines related to CCR2 biology

- Peripheral blood monocyte subset counts

Pharmacokinetics: plasma/urine drug concentrations, pharmacokinetic parameters

Safety: adverse events, vital signs, ECG-parameters, laboratory parameters,

physical examination

Secondary outcome

NA

Study description

Background summary

CCX872-B is a new investigational compound that may eventually be used for the treatment of diabetic nephropathy, a progressive kidney disease caused by chronic diabetes. This is the first time that this compound is being given to humans.

Study objective

Primair:
To evaluate the safety and tolerability of single and multiple oral doses of CCX872-B, over a range of dose levels, in healthy male and female subjects

Secundair:
To evaluate the following:
- Single and multiple dose pharmacokinetic profile of CCX872-B over a range of dose levels
- Relationship between CCX872 plasma concentrations and CCR2 receptor blockade on blood leukocytes, and
- Relationship between CCX872 plasma profile and changes in plasma MCP-1 and circulating monocyte cell counts.

Study design

Screening and follow-up:
clinical laboratory, full physical examination, ECG, vital signs; at eligibility screening: medical history, drug screen, HBsAg, anti HCV, anti-HIV 1/2 and pregnancy test (females only)

Observation period:
period 1: in clinic from -18h (Day -1) up to 24h (Day 2) after drug administration (Day 1) with ambulatory visits on Day 3, 4 and 8
period 2: in clinic from -18h (Day -1) prior to first drug administration (Day 1) up to 24h (Day 8) after last drug administration (Day 7) with an ambulatory visit on Day 15 and a follow-up phone call on Day 29.

Blood sampling:
For pharmacokinetics:
Period 1: Time 0 and at Hours 0.08 (5 minutes post dose), 0.25, 0.5, 1, 1.5, 2, 3, 4, 8, 12, and 16h after administration of study medication and once on Day 2, 3, 4 and 8
Period 2: Blood samples (4.0 mL) will be collected at Time 0 and at Hours 0.08 (5 minutes post dose), 0.25, 0.5, 1, 1.5, 2, 3, 4, 8, 12, and 16 after administration of the first dose of study medication if once daily is tested.
Blood samples (4.0 mL) collected at Time 0 and at Hours 0.25, 0.5, 1, 2, 3, 4, 8, 12, 12.25, 12.5, 13, 14, 15, and 16 after administration of the first dose of study medication if twice daily is tested.
Blood samples (4.0 mL) will be collected at Hour 24 if a once daily dosing regimen is tested, or Hours 20 and 24 if a twice daily dosing regimen is tested (Day 2), Hour 48 (Day 3), Hour 72 (Day 4), Hour 96 (Day 5), and Hour 120 (Day 6) after administration of the first dose of study medication.
Blood samples (4.0 mL) will be collected at Hours 144, 144.08 (5 minutes post dose), 144.25, 144.5, 145, 145.5, 146, 147, 148, 152, 156, and 160 (Day 7), and Hour 168 (Day 8) after administration of the first dose of study medication if once daily is tested. Blood samples (4.0 mL) will be collected at Hours 144, 144.25, 144.5, 145, 146, 147, 148, 152, 156, 156.25, 156.5, 157, 158, 159, and

160 (Day 7), and Hours 164 and 168 (Day 8) after administration of the first dose of study medication if twice daily is tested.

For pharmacodynamics:
Period 1: 2h pre-dose 2 and 24 hours post-dose
Period 2: For CCR2 receptor occupancy and internalization assays, which will only be conducted for the last 3 dose cohorts of Period 2: 1 x 10 mL plus 1 x 5 mL blood samples will be collected on Day 1, within 2 hours prior to the first CCX872-B/placebo dose and at Hour 2, 2 hours after the first CCX872-B/placebo dose, on Day 2 at Hour 24, prior to the morning dose of CCX872-B/placebo, on Day 7 at Hour 146, 2 hours after the last CCX872-B/placebo dose, and on Day 8 at Hour 168, 12 or 24 hours after the last CCX872-B/placebo dose, depending on whether twice daily or once daily dosing regimens are tested in Period 2. These PD samples will be collected at the same time as the PK sample collections. For peripheral blood monocyte subset counts: a blood sample (8 mL) will be collected within 2 hours prior to the first dose of CCX872-B/placebo on Day 1 of Period 2, on Day 7 at Hour 146 (2 hours after the morning dose on Day 7), and on Day 8, Hour 168 (12 or 24 hours after the last dose of CCX872-B/placebo, depending on the dosing regimen).

Urine sampling:
For pharmacokinetics: Day 1 at interval 0-6h (Period 1 only)

Safety assessments:
Adverse events throughout the study. Clinical laboratory, hematology, urinalysis, physical examination, vital signs, 12-lead-ECG and weight at screening and follow-up

Intervention

Period 1: subjects will receive a single dose of CCX872-B as a capsule
Period 2: subjects will receive multiple doses of CCX872-B as a capsule once or twice daily for a total of 7 days

Study burden and risks

Registration af adverse effects: During the entire investigation all adverse effect you report will be documented.
Blood draw, indwelling canula: During this study not more than 600 ml of blood will be drawn. It is anticipated that in period 1 once (Day 1) an indwelling cannula will be used and in period 2 twice (Day 1 and Day 7). The remainder of the blood draws will be drawn by direct puncture of the vein.
Collection of urine: In period 1, urine will be collected starting after dosing until 6 hours after administration of CCX872-B.
Heart trace (ECG*s): ECG*s will be made regularly: specifically on Day 1 of period 1 and on Day 1 and 7 of period 2.

Contacts

Public
Chemocentryx

Maude Avenue 850
Mountain View CA 94043
US
Scientific
Chemocentryx

Maude Avenue 850
Mountain View CA 94043
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

healthy male or female
18 - 65 years inclusive
BMI 18 - 35 kg/m2 inclusive
non-smoker

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS.
Participation in another drug study within 60 days prior to randomization.
Any donation of blood(products) or significant blood loss within 56 dagen voor de keuring.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-10-2012
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	25-10-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	26-10-2012
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2012-003737-42-NL
CCMO	NL42208.056.12