A Double-Blind, Placebo-Controlled Phase 2 Study to Evaluate the Effect of CCX140-B on Albuminuria in Subjects with Type 2 Diabetes Mellitus

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

Summary

ID

NL-OMON38004

Source
ToetsingOnline

Brief title
CCX140-B T2DM albuminuria

Condition

- Diabetic complications
- Diabetic complications
- Nephropathies

Synonym
albuminuria, protein in urine

Research involving
Human

Sponsors and support

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

Intervention

Keyword: albuminuria, CCR2 chemokine receptor, CCX140-B, type 2 diabetes mellitus

Outcome measures

Primary outcome

Urinary albumin excretion

Safety and tolerability

Secondary outcome

HbA1c

PK-parameters

Creatinine (serum, urine, clearance), blood urea nitrogen, phosphorus

Urinary MCP-1:creatinine ratio, and other serum and urinary markers of renal

function and inflammation

Study description

Background summary

Type 2 diabetes mellitus has reached epidemic proportions in the western world, and its complications are severe and disabling. One of those complications is nephropathy, slowly progressing to end stage renal failure, despite ACE-inhibitors and other therapies. Preclinical and limited clinical data suggest the immune system plays a part in the pathogenesis of the nephropathy, particularly monocytes/macrophages. In animal models, blocking of CCR2 improves renal function.

Study objective

The primary efficacy objective of this study is to evaluate the effect of

CCX140-B treatment on urinary albumin excretion in subjects with type 2 diabetes mellitus (T2DM) with albuminuria.
The primary safety objective of this study is to evaluate the safety and tolerability of CCX140-B in subjects with T2DM with albuminuria.

The secondary objectives of this study are:
1.To evaluate the effect of CCX140-B on hemoglobin A1c (HbA1c);
2.To evaluate the pharmacokinetic (PK) profile of CCX140-B in subjects with T2DM with albuminuria;
3.To evaluate the effect of CCX140-B on renal function; and
4.To evaluate the effect of CCX140-B on markers of renal function and inflammation.

Study design

Randomised, double-blind, placebo-controlled intervention

Intervention

10 mg CCX140-B or placebo once daily for 84 consecutive days.

Study burden and risks

The most commonly observed adverse events with CCX140-B were headache, fatigue, rhinorrhoea, sore throat. These symptoms were temporary. Said side effects are neither severe nor lasting. The participants contribute to the development of a novel drug against diabetic nephropathy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Male or female, aged 18-75 years inclusive, with documented previously diagnosed type 2 diabetes mellitus (per American Diabetes Association [ADA] criteria);
2.Albumin:creatinine ratio (ACR) of 100 to 3000 mg/g creatinine, inclusive, based on two values obtained from two first morning urine samples taken on two separate days during the screening period; both ACR values must be 100 to 3000 mg/g creatinine, inclusive;
3.Estimated glomerular filtration rate based on serum creatinine (eGFR, determined by Modification of Diet in Renal Disease [MDRD] equation) of >= 25 mL/min/1.73 m2;
4.All subjects must be on a stable dose of an ACE inhibitor or ARB for at least 8 weeks prior to screening. The dose of these drugs must not be lower than the lowest labeled dose. Subjects may not be on both an ACE inhibitor and an ARB. Doses of any other anti-hypertension treatment must have been stable for at least 4 weeks prior to screening. Any oral anti-diabetic treatment must have been maintained at stable dose(s) for at least 8 weeks prior to screening. If receiving insulin, must have been on insulin for at least 8 weeks prior to screening;
5.If taking any phosphate binders, cinacalcet, vitamin D or vitamin D analogues, must have been on stable doses for at least 4 weeks prior to screening;
6.Fasting plasma glucose less than 270 mg/dL at screening;
7.Willing and able to give written Informed Consent and to comply with the requirements of the study protocol;
8.Judged to be otherwise 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 (other than those specified in the Exclusion Criteria) 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; and
9.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. Adequate contraception is defined as

usage by at least one of the partners of a barrier method of contraception, together with usage by the female partner, commencing at least three months prior to Screening, of a stable regimen of any form of hormonal contraception or an intra-uterine device. Use of abstinence alone is not considered adequate. Use of a barrier method alone is considered adequate only if the male partner was vasectomized at least six months prior to Screening. Use of a double-barrier method of contraception is acceptable. Women of childbearing potential must have a negative serum pregnancy test during the screening period and a negative urine pregnancy test on the day prior to the initial dosing.

Exclusion criteria

1.Type 1 diabetes mellitus or history of diabetic ketoacidosis;
2.Previous renal transplant or known non-diabetic renal disease, except related to hypertension;
3.Has undergone renal dialysis at any time in the past;
4.Women who are pregnant or breastfeeding;
5.Body mass index (BMI) above 45.4 kg/m2;
6.Received chronic (more than 7 days continuously) systemic glucocorticoid or other immunosuppressive treatment within 8 weeks of screening;
7.Use of bardoxolone, atrasentan or other endothelin antagonist within 8 weeks of screening;
8.Received chronic (more than 7 days continuously) NSAID treatment within 2 weeks of screening;
9.Cardiac failure (class III or IV), history of unstable angina, symptomatic coronary artery disease, myocardial infarction or stroke within 12 weeks of screening;
10.Poorly-controlled blood pressure (systolic blood pressure >155 or diastolic blood pressure >95, with blood pressure measured in the seated position after at least 5 minutes of rest);
11.History of hypersensitivity to ingredients of the placebo (tartrazine, microcrystalline cellulose, starch, or croscarmellose sodium);
12.History or presence of leukopenia (WBC count <3.5 x 109/L);
13.History or presence of any form of cancer within the 5 years prior to randomization, with the exception of excised basal cell or squamous cell carcinoma of the skin, or cervical carcinoma in situ or breast carcinoma in situ that has been excised or resected completely and is without evidence of local recurrence or metastasis;
14.Presence of tuberculosis based on chest X rays, tuberculin skin test, QuantiFERON®-TB Gold test, or T-SPOT®.TB test performed during screening; If screening test is performed and it is deemed positive due to previous vaccination or TB exposure, chest X rays must be acquired to rule out TB;
15.Positive HBV, HCV, or HIV viral screening test;
16.History of gastrointestinal conditions that may interfere with study medication compliance, e.g., severe gastroparesis, with regurgitation of food or oral medication;
17.History of alcohol or illicit drug abuse;
18.Any infection requiring antibiotic treatment within 4 weeks of screening;
19.Hemoglobin less than 10 g/dL (or 6.18 mmol/L) at screening;
20.Evidence of hepatic disease; AST, ALT, or bilirubin > 2 x the upper limit of normal;
21.Clinically significant abnormal ECG during screening, e.g., QTc greater than 450 msec;

22.Participation in another clinical trial within 3 months prior to the start of this study or more than 4 times per year; and
23.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.

Study design

Design

Study phase:	2
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):	18-10-2011
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CCX140-B
Generic name:	4-Chloro-N-[5-methyl-2-(7H-pyrrolo[2,3-d]pyrimidin-4-ylcarbonyl)-3-pyridinyl]-3-(trifluoromethyl)-be

Ethics review

Approved WMO

Date:	29-07-2011
Application type:	First submission

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	29-08-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-10-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	24-04-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	02-05-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	28-08-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2011-003049-16-NL
CCMO	NL37590.058.11