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Study to evaluate the safety and efficacy of CCX168 in subjects with renal vasculitis on background cyclophosphamide treatment

Submission date	Recruitment status	[_] Prospectively registered
09/07/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
25/08/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
21/01/2019	Circulatory System	

Plain English summary of protocol

Background and study aims
ANCA-associated renal vasculitis (AARV) is an autoimmune disease involving multiple organs including the kidneys. It is caused by abnormal antibodies (autoantibodies) that attack a certain type of white blood cells (neutrophils) and can cause those neutrophils to stick to and destroy the inside walls of small blood vessels in tissue and organs such as the kidney. ANCA is an acronym for Anti-Neutrophil Cytoplasmic Antibody.
The aim of this study is to test a newly developed drug (oral investigational product CCX168) for safety and tolerability while you continue to receive the standard of care cyclophosphamide treatment, and varying doses of prednisone or prednisone placebo.

Who can participate?
Patients aged 18-75 who are experiencing a recent relapse or new diagnosis of ANCA-associated renal vasculitis.

What does the study involve?
Some patients will receive capsules of CCX168 or placebo, and capsules of prednisone or prednisone-placebo daily for a period of 84 days. This is in addition to their standard of care intravenous cyclophosphamide treatment.

What are the possible benefits and risks of participating?
If successful, CCX168 could possibly allow for lower dosing or complete elimination of high dose corticosteroid treatment in this disease. As a result patients with this disease may have less of the toxic side effects usually caused by high dose corticosteroids. CCX168 appeared to be well tolerated in Phase I studies with healthy subjects and adverse events were mild in nature. All new drugs (investigational compounds) have the potential for unanticipated serious or life-adverse events. These side effects could be in addition to the well documented side effects of cyclophosphamide and high dose corticosteroid standard of care treatments.

Where is the study run from?
There are about 40 sites participating in this study. They are located in Belgium, Czech Republic,

Germany, Hungary, the Netherlands, Poland, Sweden and the UK. The lead study center is at Addenbrookes Hospital, Department of Nephrology at Cambridge in the UK.

When is the study starting and how long is it expected to run for?
Patient screening and dosing are scheduled to begin in the fall of 2011 completing in December 2012.

Who is funding the study?
ChemoCentryx (USA)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01363388

Protocol serial number
CL002_168

Study information

Scientific Title
A randomized, double-blind, placebo-controlled, phase 2 study to evaluate the safety and efficacy of CCX168 in subjects with renal vasculitis on background cyclophosphamide treatment

Acronym
CLEAR (C5aR inhibitor on Leukocytes Exploratory ANCA-associated Renal vasculitis study)

Study objectives

That CCX168, a C5a complement receptor, will be safe, well tolerated and effective in patients with antineutrophil cytoplasmic antibodies ANCA-associated renal vasculitis on background cyclophosphamide treatment and may result in reduced toxicity of induction therapy by the reduction of or the elimination of systemic corticosteroid therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East of England-Cambridge Central, 13/10/2011, ref: 11/EE/0210
All other centres will seek ethics approval before recruitment of the first participant

Study design
Multi-centre randomized double-blind placebo-controlled phase 2 study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Renal Vasculitis

Interventions
1. Treatment: CCX168 30mg or placebo twice daily for 84 days
2. Comparator: Prednisone at starting doses ranging from 15 to 60 mg (body weight dependent) per day for 84 days or matching prednisone placebo once daily for 84 days

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
CCX168, prednisone, cyclophosphamide

Primary outcome(s)
Safety of CCX168 in patients with anti-neutrophil cytoplasmic antibody associated renal vasculitis measured upon completion of 84 days of treatment.

Key secondary outcome(s))
Systemic corticosteroid use measured upon completion of 84 days of treatment.

Completion date
31/03/2013

Eligibility

Key inclusion criteria
1. Clinical diagnosis of Wegeners granulomatosis, microscopic polyangiitis or renal limited vasculitis
2. Male and postmenopausal or surgically sterile female subjects, aged 18-75 years with new or relapsed ANCA-associated renal vasculitis (AARV) where treatment with cyclophosphamide would be required
3. Positive indirect immunofluorescence (IIF) test for peri-nuclear (protoplasmic-staining) antineutrophil cytoplasmic antibodies (P-ANCA) or C-ANCA, or positive Enzyme-linked immunosorbent assay (ELISA) test for anti-proteinase-3 (PR3) or anti-myeloperoxidase (MPO) at screening
4. Proven to have renal vasculitis based on renal biopsy or have hematuria and proteinuria compatible with nephritis
5. Estimated glomerular filtration rate of greater than 30 mL per minute

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Key exclusion criteria
1. Severe disease as determined by rapidly progressive glomerulonephritis, alveolar hemorrhage, hemoptysis, rapid-onset mononeuritis multiplex or central nervous system involvement
2. Any other multi-system autoimmune disease
3. Medical history of coagulopathy or bleeding disorder
4. Received cyclophosphamide within 12 weeks of screening; if on azathioprine, mycophenolate mofetil, or methotrexate at the time of screening, these drugs must be withdrawn prior to receiving the cyclophosphamide dose on Day 1
5. Received high-dose intravenous corticosteroids within 4 weeks of screening
6. On an oral dose of a corticosteroid of more than 10 mg prednisone-equivalent at the time of screening
7. Received rituximab or other B-cell antibody within 52 weeks of screening or 26 weeks provided B cell reconstitution has occurred; received anti-TNF treatment, abatacept, alemtuzumab, intravenous immunoglobulin (IVIg), or plasma exchange within 12 weeks of screening

Date of first enrolment
01/08/2011

Date of final enrolment
31/03/2013

Locations

Countries of recruitment
United Kingdom

England

Belgium

Czech Republic

Germany

Hungary

Netherlands

Poland

Sweden

Study participating centre
Addenbrooke's Hospital
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
ChemoCentryx, Inc. (USA)

ROR
https://ror.org/04gp12571

Funder(s)

Funder type
Industry

Funder Name
ChemoCentryx, Inc. (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/09/2017	21/01/2019	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes