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Clinical trial to evaluate the safety and efficacy of CCX168 in ANCA-associated vasculitis (AAV)

Submission date
06/10/2014

Recruitment status
No longer recruiting

Registration date
17/11/2014

Overall study status
Completed

Last Edited
19/04/2021

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
ANCA (Anti-Neutrophil Cytoplasmic Antibody)-associated renal vasculitis (AAV) 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 cell (neutrophils) and can cause those neutrophils to stick to and destroy the inside walls of small blood vessels in tissue and internal organs. Standard treatment for the condition includes cyclophosphamide or rituximab plus corticosteroids. However, the complement C5a receptor CCX168 has been shown to work in mice suffering from ANCA-induced glomerulonephritis and there are encouraging results from another clinical trial involving patients with AAV. Here, we want to compare the safety and performance of two different doses of CCX168 in patients with AAV. while they continue to receive the standard of care (SOC) IV cyclophosphamide treatment, and varying doses of a prednisone or prednisone placebo.

Who can participate?
Adults aged at least 18 diagnosed with AAV.

What does the study involve?
Participants are randomly allocated to one of three groups. Those in group A are given 20mg CCX168 twice a day plus their SOC treatment for 12 weeks. Those in group B are given 30mg of CCX168 twice a day plus their SOC treatment for 12 weeks. Those in group C are given a placebo twice a day plus their SOC treatment for 12 weeks. This is followed by a 12 week follow-up period assessing the success of the treatment.

What are the possible benefits and risks of participating?
CCX168 has already been tested on healthy subjects in one study and patients with AAV in another. One of the purposes of this research study is to investigate the effects of CCX168 on vasculitis (AAV) disease activity in patients. It is possible that CCX168 may have a beneficial effect. However, there is no guarantee that any individual participant will be given CCX168 rather than placebo in this study, and there is no guarantee that CCX168 will be beneficial in the treatment of their condition. The most common side effects are headache, diarrhoea, dizziness, lower abdominal pain, nausea, vomiting, and sore throat.

Where is the study run from?
Chemocentryx (USA)

When is the study starting and how long is it expected to run for?
September 2014 to September 2019

Who is funding the study?
Chemocentryx (USA)

Who is the main contact?
Ms Antonia Potarca
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT02222155

Protocol serial number
CL003_168

Study information

Scientific Title
A randomized, double-blind, placebo-controlled, dose assessment Phase 2 study to evaluate the safety and efficacy of CCX168 in subjects with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis

Acronym
CLASSIC (Clinical ANCA Vasculitis Safety and Efficacy Study of Inhibitor of C5aR)

Study objectives
Test whether CCX168 plus standard of care treatment is safe and efficacious in patients with AAV.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Sterling IRB, Atlanta, Georgia, 26/08/2014, IRB ID#: 4839-001

Primary study design
Interventional

Study design
Randomized double-blind placebo-controlled Phase 2 study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
ANCA-associated vasculitis (AAV)

Interventions
CCX168 (10 or 30 mg) twice daily plus standard of care (cyclophosphamide/rituximab plus corticosteroids). Following the 84-day dosing period, there will be an 84-day follow-up period.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Safety and efficacy of CCX168 in subjects with AAV on SOC cyclophosphamide or rituximab plus corticosteroid treatment. Efficacy is evaluated based on the Birmingham Vasculitis Activity Score (BVAS). BVAS assessments will be made on Days 1, 29, 85, 113, and 169.

Key secondary outcome(s)
1. Efficacy of CCX168 compared to SOC based on changes in eGFR, Hematuria and Albuminuria will be assessed on Days 1, 2, 8, 15, 22, 29, 43, 57, 71, 85, 99, 113, 141, and 169.
2. Assessment of changes in renal inflammatory activity based on MCP-1:creatinine ratio and serum C-reactive protein concentrations with CCX168 compared to SOC will be completed on Days 1 (prior to dosing), 8, 15, 29, 57, 85, 113, and 169.
3. Assessment of health-related quality-of-life changes based on SF-36v2 and EQ-5D-5L with CCX168 compared to SOC will completed on Days 1, 29, 85, and 169.
4. Assessment of changes in VDI with CCX168 compared to SOC, made on Days 1, 85, and 169.
5. Assessment of changes in ANCA (anti-PR3 and anti-MPO) with CCX168 compared to SOC will be made on Days 1 (prior to dosing), 29, 85, 113, and 169.

Completion date
30/09/2016

Eligibility

Key inclusion criteria
1. Male or female subjects 18 years and older, with new or relapsed AAV
2. Clinical diagnosis of granulomatosis with polyangiitis (Wegeners), microscopic polyangiitis or renal limited vasculitis
3. Female subjects of childbearing potential, and male subjects with partners of childbearing potential may participate in the study if adequate contraception is used
4. Positive indirect immunofluorescence (IIF) test for P-ANCA or C-ANCA, or positive ELISA test for anti-proteinase-3 (PR3) or anti-myeloperoxidase (MPO) at screening
5. Have at least one 'major' item, or at least three other items, or at least two renal items on the Birmingham Vasculitis Activity Score (BVAS) version 3
6. Estimated glomerular filtration rate (eGFR) ≥ 20 mL per minute

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
42

Key exclusion criteria
1. Severe disease as determined by rapidly progressive glomerulonephritis or alveolar hemorrhage
2. Any other multi-system autoimmune disease
3. Medical history of coagulopathy or bleeding disorder
4. Received cyclophosphamide with 12 weeks prior to screening; if on azathioprine, mycophenolate mofetil, or methotrexate at the time of screening, these drugs must be withdrawn prior to receiving the cyclophosphamide or rituximab dose on Day 1
5. Received intravenous corticosteroids, >3000 mg methylprednisolone equivalent, within 12 weeks prior to screening
6. Received an oral daily dose of a corticosteroid of more than 10 mg prednisone-equivalent for more than 6 weeks continuously prior to the screening visit
7. Received rituximab or other B-cell antibody within 52 weeks of screening or 26 weeks provided B cell reconstitution has occurred; received anti-tumor necrosis factor (TNF) treatment, abatacept, alemtuzumab, intravenous immunoglobulin (IVIg), belimumab, tocilizumab, or plasma exchange within 12 weeks prior to screening
8. Symptomatic congestive heart failure requiring prescription medication, peripheral edema of cardiac origin, poorly-controlled hypertension, history of unstable angina, myocardial infarction or stroke within 6 months prior to screening
9. History or presence of any form of cancer within the 5 years prior to screening
10. Evidence of tuberculosis based on chest X rays

11. Positive HBV, HCV, or HIV viral screening test
12. Any infection requiring antibiotic treatment within 4 weeks prior to screening
13. Received a live vaccine within 4 weeks prior to screening
14. WBC count less than 4000/µL, or neutrophil count less than 2000/µL, or lymphocyte count less than 1000/µL
15. Hemoglobin less than 9 g/dL at screening
16. Evidence of hepatic disease
17. Prothrombin time (PT) or partial thromboplastin time (PTT) above the normal reference limit
18. Clinically significant abnormal ECG during screening
19. Participated in any clinical study of an investigational product within 30 days prior to screening
20. 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

Date of first enrolment
01/09/2014

Date of final enrolment
30/09/2016

Locations

Countries of recruitment
Canada

United States of America

Study participating centre
850 Maude Ave.
Mountain View
United States of America
94043

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 provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/11/2020	19/04/2021	Yes	No
Abstract results	results presented at ACR/ARHP :	28/09/2016	15/04/2019	No	No