ADVOCATE (CL010_168)

A randomized, double-blind, placebo-controlled, phase 3 study to evaluate the safety and efficacy of avacopan (CCX168) in patients with ANCA-associated vasculitis treated concomitantly with rituximab or cyclophosphamide/azathioprine.

Sponsor: Chemocentryx
Mount Sinai Hospital - Site Activation: June 2017
Site Primary Investigator: Dr. Christian Pagnoux (christian.pagnoux@sinaihealthsystem.ca)
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Objective and Background:
To evaluate the efficacy of avacopan to induce and sustain remission when used in combination with CYC/AZA or RITUX in patients with active newly-diagnosed or relapsing ANCA-associated vasculitis.

Study Design:
- Phase 3 randomized, double-blind, double-dummy, placebo controlled trial for 52 weeks followed by an 8 week follow up period.
- *Stratification factors:*
1. Treatments:
   I. IV RITUX – 4 weekly infusions
   II. IV CYC – 6 infusions at specific intervals followed by oral AZA at week 15
   III. PO CYC daily followed by oral AZA at week 15
2. PR3 vs. MPO disease
3. Newly diagnosis vs. relapsing disease
- *Randomization* in a 1:1 ratio to one of two groups:
- *Group A:* Placebo avacopan + CYC/AZA or RITUX with full starting dose of prednisone
- *Group B:* avacopan + CYC/AZA or RITUX with placebo prednisone
- avacopan or placebo PO taken in the morning and 12 hours later in the evening with food
- Prednisone and placebo-prednisone tapered according to protocol, and stopped at week 20
- *Endpoint:* patients achieving remission at week 26 (off prednisone) and maintaining remission until week 52

Needed number of patients to enroll:
Approximately 300 patients will be enrolled

Inclusion Criteria:
1. Age ≥ 18 years
2. Newly-diagnosed or relapsed GPA or MPA where treatment with CYC or RITUX is needed
3. Current or historic PR3 or MPO-ANCA + result
4. BVAS: 1 major or ≥3 minor or ≥ proteinuria and hematuria
5. eGFR ≥ 15ml/min/1.73m^2 at screening

Exclusion criteria:
1. Other known multi-system auto-immune disease or have had a kidney transplant
2. Required dialysis, plasma exchange or CYC 12 weeks prior to screening or >3000 mg of IV methylprednisolone 4 weeks prior to screening or RITUX within 52 weeks to screening
3. Taking PO prednisone of >10mg for more than 6 continuous weeks prior to screening
4. If on AZA, MMF, MTX, these drugs need to be stopped prior to on Day 1
5. Active cancer/history of malignancy within 5 years prior to screening
6. Positive HBV, HCV or HIV within 6 weeks of screening or received a live vaccine with 4 weeks of screening
7. Abnormal laboratory results prior to dosing or previous participation in CCX168 study
8. Pregnant/breast-feeding women

For more information on the study or enrollment procedure, please contact study site PI, sub-I or study coordinator using emails above, or by phone at 416-586-4800 ext. 8549 or 5519 or 2210

Study Schema for ADVOCATE Trial