ABROGATE

Abatacept (CTLA4-Ig) for the treatment of
relapsing, non-severe, Granulomatosis with Polyangiitis (Wegener's)

Sponsor: VCRC - Tampa, FL – Dr. Carol Langford (PI)
Funding: National Institutes of Health and Bristol-Myers Squibb

Mount Sinai Hospital - Site Activation: May 2015
Site Primary Investigator: Dr. Christian Pagnoux (cpagnoux@mtsinai.on.ca)
Site Sub-Investigator: Dr. Simon Carette (simon.carette@uhn.ca)
Study Coordinator: Samyukta Jagadeesh (sjagadeesh@mtsinai.on.ca)

Objective and Background:
To evaluate the efficacy of abatacept to achieve sustained glucocorticoid-free remission in patients with relapsing non-severe GPA

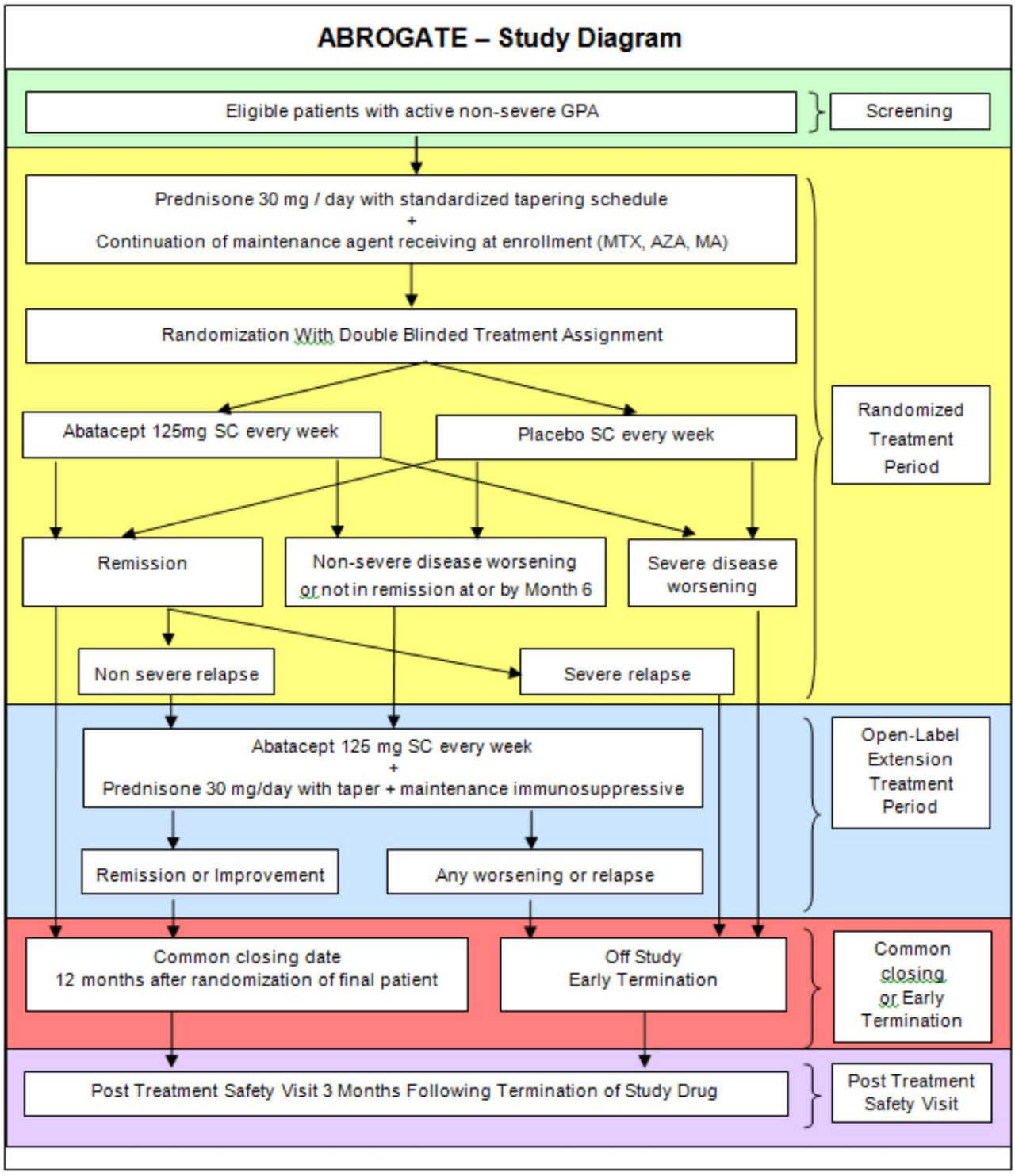
Study Design:
- Double-blinded placebo controlled study
- Eligible patients are those patients with relapsing non-severe GPA (no major item on the BVAS/WG) within 28 days prior to screening
- Enrolled subjects will be randomized in a 1:1 ratio to receive SC abatacept 125 mg qw + prednisone or SC placebo qw + prednisone
- Randomization and initiation of drug/placebo must occur within 2 weeks of the screening visit
- Endpoint is the ability of abatacept to reduce the treatment failure rate through 12 months
- Open label trial period is an option for patients who experience non-severe relapse (increase or new development in the BVAS/WG) or who have not achieved remission by month 6 (BVAS/WG = 0 or 1)

Needed number of patients to enroll:
Objective is to enroll 136 into the study
Hypothesis is a flare rate of 60% in the placebo arm at month 12 versus 30% or less in the abatacept arm

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

Inclusion Criteria:
1. GPA with ≥2/5 modified ACR criteria
   a. Nasal or oral inflammation
   b. Abnormal chest radiograph
   c. Active urinary sediment (microscopic hematuria or RBC casts)
   d. Granulomatous inflammation on biopsy
   e. Positive ANCA test measured by ELISA
2. Relapse of GPA within 28 days prior to screening with
   a. No major elements in the BVAS/WG
   b. No immediate threat to any critical organ system or life
3. Age ≥ 18 years

Exclusion Criteria:
1. Treatment with CYC or initiation/dose change of maintenance therapy (MTX, AZA, MA) within the 3 months prior to screening
2. Treatment with ≥1000 mg methylprednisolone within the 28 days prior to screening OR >30mg OD prednisone for >28 days prior to screening
3. History of malignancy within the last 5 years
4. Having received an investigational product within 30 days or infliximab, etanercept, adalimumab, belimumab or tocilizumab within 3 months prior to enrollment
5. Treatment with rituximab within the past 6 months
6. eGFR <20 ml/min
7. Live vaccination fewer than 3 months prior to enrollment
8. Active TB (even if treated) or latent TB (unless treated for >4 weeks prior to randomization)


ABROGATE – Study Diagram
Eligible patients with active non-severe GPA
Screening
Prednisone 30 mg / day with standardized tapering schedule
+
Continuation of maintenance agent receiving at enrollment (MTX, AZA, MA)
Randomization With Double Blinded Treatment Assignment
Abatacept 125mg SC every week
Placebo SC every week
Randomized Treatment Period
Remission
Non-severe disease worsening or not in remission at or by Month 6
Severe disease worsening
Non severe relapse
Severe relapse
Abatacept 125 mg SC every week
+
Prednisone 30 mg/day with taper + maintenance immunosuppressive
Open-Label Extension Treatment Period
Remission or Improvement
Any worsening or relapse
Common closing date
12 months after randomization of final patient
Off Study
Early Termination
Common closing or Early Termination
Post Treatment Safety Visit 3 Months Following Termination of Study Drug
Post Treatment Safety Visit