For information regarding the Rituximab treatment for ANCA-Associated vasculitis, contact:

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For further detailed information, go to our web-site: http://vasculitis.med.jhu.edu

Other Centers Participating in this Trial Include:

Mayo Clinic
Cleveland Clinic
Boston University
Duke University
University of Alabama at Birmingham
University of California at San Francisco
Hospital of Special Surgery, New York

THE JOHNS HOPKINS
Vasculitis Center

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If you are interested in knowing more about how you can support the missions of The Johns Hopkins Vasculitis Center in research, teaching, and patient care, please contact:

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Visit our website at:
http://vasculitis.med.jhu.edu

RAVE

Rituximab for ANCA-Associated Vasculitis

Sponsored by The National Institute of Allergy and Infectious Disease and The Immune Tolerance Network

The Johns Hopkins Vasculitis Center

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JHAAC Room 1B.1A
Baltimore, MD 21224

Scheduling Telephone: (410) 550-6825
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STUDY DESIGN

Projected Enrollment 200 Patients

Trial will consist of two phases.

• A 6-month remission induction

Control arm will receive daily oral prednisone, daily oral CYC for 3-6 months, and rituximab-placebo infusions.

Experimental arm will receive daily oral prednisone, daily oral CYC-placebo for 3-6 months, and rituximab infusions.

• 12-month remission maintenance phase.

Control arm will discontinue CYC and start oral azathioprine daily, up to month 18.

Experimental arm will discontinue CYC placebo and start azathioprine placebo daily, up to month 18.

In the event of a severe flare before month 6, patients will be crossed-over to the opposite treatment arm and will undergo the remission induction treatment of that treatment arm.

Patients who develop a severe flare between month 6 and month 18 will be treated open-label with rituximab and glucocorticoids for remission induction.

All participants will be followed until 18 months after enrollment of the last patient. After the month 18 study visit, participants will be treated according to best medical judgment.

Inclusion Criteria

Must be over 15 years of age

Must weigh at least 40 kg (88 lbs)

Must have diagnosis of Wegener's Granulomatosis or Microscopic Polyangiitis
(Chapel Hill Consensus Conference)

Newly diagnosed, or disease flare

Disease activity: BVAS/WG ≥ 3

Disease severity: that requires treatment with CYC

Must be positive for either PR3-ANCA or MPO-ANCA at screening

Willing to practice contraception during trial and 1 year following participation

Breastfeeding contract: If female, must be willing to refrain from breastfeeding throughout trial

Must be willing to comply with study procedures

Must be willing and able to provide informed consent

Exclusion Criteria

Churg Strauss syndrome

Limited disease that would not normally be treated with CYC

Patient requiring mechanical ventilation because of alveolar hemorrhage

History of severe allergic reactions to human or chimeric monoclonal antibodies, or murine protein

Systemic infection, osteomyelitis, septic arthritis, pneumonia complicated by empyema, or lung abscesses; within 6 months of randomization

Active hepatitis B or C, or documented history of HIV or hepatitis B or C

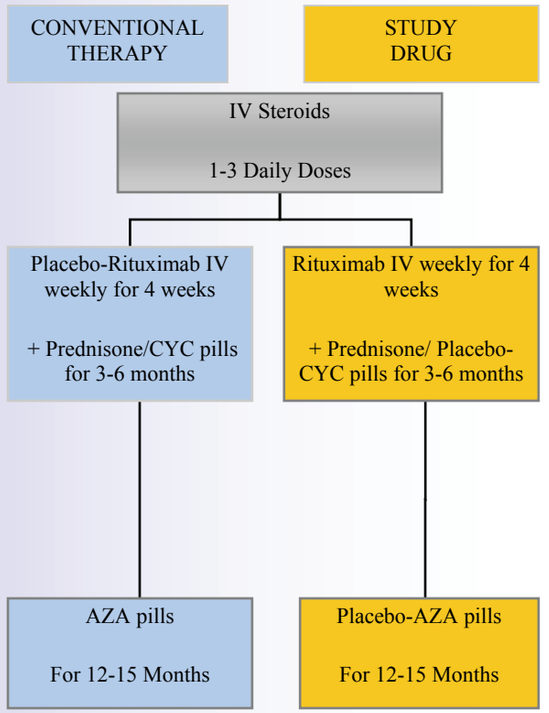
Liver disease sufficiently severe to impair ability to participate in the trial

Anti-GBM disease

Malignancy: active or history of malignancy in last 5 years. Squamous cell or basal cell skin carcinomas and individuals with cervical carcinoma in situ may be enrolled, if curative surgical treatment has been received

Uncontrolled disease, or evidence of other disease (i.e. drug and alcohol abuse) that could interfere with study participation

STUDY SCHEMA



IF A PATIENT FLARES BEFORE MONTH 6 THE PATIENT WILL "CROSSOVER" TO THE OTHER TREATMENT ARM.

IF A PATIENT FLARES AFTER 6 MONTHS, THEN OPEN-LABEL RITUXIMAB OR BEST MEDICAL JUDGEMENT WILL GUIDE TREATMENT.

PLEASE REFER YOUR PATIENT AS SOON AS POSSIBLE. THERE IS A NARROW TIME WINDOW ONCE CYCLOPHOSPHAMIDE AND PREDNISONE ARE STARTED (1-2 WEEKS).