

# An international, randomised, open label trial comparing a rituximab-based regimen with a standard cyclophosphamide/azathioprine based regimen in the treatment of active, generalised anti-neutrophilic cytoplasmic antibodies associated vasculitis

<b>Submission date</b> 21/09/2005	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 13/03/2006	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 06/03/2015	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

## Study information

**Scientific Title**

An international, randomised, open label trial comparing a rituximab-based regimen with a standard cyclophosphamide/azathioprine based regimen in the treatment of active, generalised anti-neutrophilic cytoplasmic antibodies associated vasculitis

**Acronym**

RITUXVAS

**Study objectives**

Rituximab leads to a higher rate of sustained remission compared to standard therapies (cyclophosphamide/azathioprine) with a lower rate of severe adverse events and reduced cyclophosphamide exposure

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Not provided at time of registration

**Study design**

Randomised controlled trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

ANCA-associated vasculitis

**Interventions**

Drug regimens:

1. Rituximab regimen: rituximab, 375 mg/m<sup>2</sup> IV once a week for four weeks (i.e. four doses total), with two doses of cyclophosphamide 15 mg/kg, two weeks apart given with the first and third rituximab dose
2. Control (cyclophosphamide/azathioprine) regimen: cyclophosphamide 15 mg/kg for 3-6 months (6-10 doses total) to be given intravenously according to protocol for remission induction. Cyclophosphamide should be converted to azathioprine for remission maintenance.
3. Steroids: all patients will receive 1 g IV methylprednisolone, then same daily oral corticosteroid regimen
4. Plasma exchange or IV methylprednisolone will be allowed according to local practice for patients with organ threatening disease. Randomisation should not occur until completion of plasma exchange to avoid loss of rituximab during plasma exchange. The first dose of cyclophosphamide can be given prior to completion of plasma exchange.

**Intervention Type**

Drug

**Phase**

Not Applicable

## **Drug/device/biological/vaccine name(s)**

Rituximab, cyclophosphamide, azathioprine

## **Primary outcome(s)**

1. Sustained remission (Birmingham Vasculitis Assessment Score [BVAS] = 0 at six months and sustained for six months)
2. Severe adverse events (Common Terminology Criteria for Adverse Events [CTCAE] grade  $\geq 3$ ) at two years

## **Key secondary outcome(s)**

1. Efficacy
  - 1.1. Response rate at six weeks (BVAS <50% baseline)
  - 1.2. Remission at six months (BVAS = 0 for 2 months by 6 months)
  - 1.3. Time to remission (BVAS = 0)
  - 1.4. Relapses (all relapses and major or minor)
  - 1.5. BVAS area under the curve
  - 1.6. Change in Glomerular Filtration Rate (GFR)
  - 1.7. Change in SF-36
  - 1.8. Change in Venous Distensibility Index (VDI)
2. Safety
  - 2.1. Severe adverse events (CTCAE grade  $\geq 3$ ) at six weeks and six months
  - 2.2. All adverse events
  - 2.3. Death
  - 2.4. Prednisolone cumulative dose
  - 2.5. Cyclophosphamide cumulative dose

## **Completion date**

01/11/2008

## **Eligibility**

### **Key inclusion criteria**

1. A new diagnosis of Wegener's Granulomatosis (WG), Microscopic Polyangiitis (MP) or Renal-Limited Vasculitis (RLV)
2. Renal involvement attributable to active WG, MP or RLV with at least one of the following:
  - 2.1. Biopsy demonstrating necrotizing glomerulonephritis
  - 2.2. Red cell casts on urine microscopy or  $\geq ++$  haematuria
3. Anti-Neutrophilic Cytoplasmic Antibodies (ANCA) positivity; ANCA positivity requires either:
  - 3.1. Proteinase 3 anti-neutrophilic cytoplasmic antibody (PR3-ANCA) by Enzyme-Linked Immunosorbent Assay (ELISA) or a typical antineutrophil cytoplasmic antibody (cANCA) pattern by indirect immunofluorescence (IIF), or both
  - 3.2. Myeloperoxidase- anti-neutrophilic cytoplasmic antibody (MPO-ANCA) by ELISA. A positive perinuclear anti-neutrophilic cytoplasmic antibody (pANCA) by IIF requires confirmation by MPO-ANCA ELISA
4. Written informed consent

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

**Age group**

Adult

**Sex**

All

**Key exclusion criteria**

1. Previous cyclophosphamide, (greater than two weeks of an oral or intravenous [IV] pulse cyclophosphamide regimen)
2. Co-existence of another multisystem autoimmune disease, e.g. SLE, Churg Strauss syndrome, Henoch Schonlein purpura, rheumatoid vasculitis, essential mixed cryoglobulinaemia, anti-glomerular basement membrane antibody positivity
3. Hepatitis B antigen positive or hepatitis C antibody positive
4. Known HIV positive (HIV testing will not be a requirement for this trial)
5. Previous malignancy (usually exclude unless agreed with trial co-ordinator)
6. Pregnancy, breast feeding or inadequate contraception if female
7. Allergy to a study medication
8. Live vaccine within last four weeks

**Date of first enrolment**

01/11/2005

**Date of final enrolment**

01/11/2008

**Locations**

**Countries of recruitment**

United Kingdom

England

Australia

Czech Republic

Germany

Mexico

Netherlands

Sweden

Switzerland

**Study participating centre**

**Addenbrooke's Hospital**  
Cambridge  
United Kingdom  
CB2 2QQ

## Sponsor information

### Organisation

Cambridge University Hospitals NHS Foundation Trust (UK)

### ROR

<https://ror.org/04v54gj93>

## Funder(s)

### Funder type

Industry

### Funder Name

Research grant provided by Hoffman La Roche to investigator own account - vasculitis research account

## 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?
<a href="#">Results article</a>	results	15/07/2010		Yes	No
<a href="#">Results article</a>	results	01/06/2015		Yes	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes