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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

Submission date 21/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 13/03/2006	**Overall study status** Completed	
Last Edited 06/03/2015	**Condition category** Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.vasculitis.org

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

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

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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

Interventions
Drug regimens:
1. Rituximab regimen: rituximab, 375 mg/m2 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 measure
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 ≥3) at two years

Secondary outcome measures
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 ≥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

Overall study start date
01/11/2005

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 ≥++ 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

Age group
Adult

Sex
Both

Target number of participants
40

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
Australia

Czech Republic

England

Germany

Mexico

Netherlands

Sweden

Switzerland

United Kingdom

Study participating centre
Addenbrooke's Hospital
Cambridge
United Kingdom
CB2 2QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust (UK)

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Sponsor type
Hospital/treatment centre

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

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	results	15/07/2010		Yes	No
Results article	results	01/06/2015		Yes	No