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Plasma exchange and glucocorticoid dosing in the treatment of antineutrophil cytoplasm antibody associated vasculitis

Submission date
01/06/2009

Recruitment status
No longer recruiting

Registration date
22/06/2009

Overall study status
Completed

Last Edited
27/09/2022

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Severe, antineutrophil cytoplasm antibody associated vasculitis (AAV) is an uncommon disease of the immune system diagnosed in about 1430 per 100,000 people in the UK each year. It is caused by caused by abnormal antibodies that attack the body's own cells and tissues. AAV is important because it carries a poor prognosis, with up to half of patients dying or developing kidney failure within 5 years. Two major problems hinder the treatment of AAV: a lack of treatment strategies to bring the disease under control quickly before it causes major organ damage, and a high degree of treatment-related toxicity (side effects). The aim of this study is to examine these problems in patients with severe AAV.

Who can participate?
Patients aged 15 or over with severe AAV

What does the study involve?
Participants are randomly allocated to either receive plasma exchange (a method of rapidly removing the abnormal antibodies), or to not receive plasma exchange. Participants are also randomly allocated to receive either a standard dose of steroids or a low-dose scheme which is predicted to reduce treatment-related toxicity.

What are the possible benefits and risks of participating?
By addressing these problems we hope to significantly improve patient survival and reduce the frequency of kidney failure in patients with AAV.

Where is the study run from?
Addenbrooke's Hospital (UK)

When is the study starting and how long is it expected to run for?
November 2009 to July 2018

Who is funding the study?
Health Technology Assessment Programme (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2009-013220-24

ClinicalTrials.gov (NCT)
NCT00987389

Protocol serial number
HTA 08/56/04; PEXIVASv1.0

Study information

Scientific Title
Plasma exchange and glucocorticoid dosing in the treatment of antineutrophil cytoplasm antibody associated vasculitis: an international randomised controlled trial

Acronym
PEXIVAS

Study objectives
This is a two-by-two factorial design randomised controlled trial and has two primary hypotheses:
1. Plasma exchange in addition to immunosuppressive therapy and glucocorticoids will reduce death and end-stage renal disease (ESRD) compared to immunosuppression and glucocorticoids

alone in patients with antineutrophil cytoplasm antibody (ANCA) associated vasculitis
2. A reduced dose glucocorticoids regimen will be non-inferior to a standard regimen with respect to death and ESRD in patients with ANCA associated vasculitis

More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/085604
Protocol can be found at: http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0011/53012/PRO-08-56-04.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Board: NRES Committee London – Harrow, 30/10/2009, Ref: 09/H0709/56

Study design
Two-by-two factorial design randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Anti-neutrophil cytoplasm antibody associated vasculitis (AAV) with nephritis or lung haemorrhage

Interventions
1. Plasma exchange (seven exchanges of human albumin at a dose of 60 ml/kg over 14 days) as an adjunctive therapy to standard immunosuppression treatment and glucocorticoids
2. A reduced dose glucocorticoid tapering regimen compared to a standard dose glucocorticoid tapering regimen

Intervention Type
Mixed

Primary outcome(s)
Death or end-stage renal disease. Timepoint for all analyses is the common closeout date (2 years after the last patient is enrolled).

Key secondary outcome(s))
Current secondary outcome measures, as of 21/03/2018:
1. Sustained remission will be analyzed by comparing the difference in proportions (and associated 95% confidence intervals) of patients that achieve a sustained remission in each treatment group.
2. Death and ESRD will be analyzed separately in an identical manner to the composite primary endpoint.
3. Safety analyses will be performed by assessing the 95% confidence interval of the rate difference of serious adverse events between treatment groups.
4. The rate of serious infections will be assessing the 95% confidence interval of the rate difference between the treatment groups both for the first year and at trial end.

5. Health-related quality of life using the SF-36 Physical Composite, Mental Composite and EQ-5D Index Score.
Patients were seen at Week 26, Week 52 and then every 6 months until study end.

Previous secondary outcome measures:
1. Disease activity (measured with the Birmingham Vasculitis Activity Score 2003)
2. Health related quality of life (measured with the EuroQoL EQ5D index score and 36-item Short Form Health Survey)
3. Serious adverse events

Timepoint for all analyses is the common closeout date (2 years after the last patient is enrolled).

Completion date
31/07/2018

Eligibility

Key inclusion criteria
1. New or previous clinical diagnosis of Wegener's granulomatosis, or microscopic polyangiitis consistent with the Chapel-Hill consensus definitions
2. Positive test for proteinase 3-ANCA or myeloperoxidase-ANCA
3. Severe vasculitis defined by at least one of the following:
3.1. Renal involvement, characterised by:
3.1.1. Renal biopsy demonstrating focal necrotising glomerulonephritis or active urine sediment demonstrating glomerular haematuria/red cell casts and proteinuria, and
3.1.2. Estimated glomerular filtration rate (eGFR) less than 50 ml/min/1.73 m2), or
3.2. Pulmonary haemorrhage due to active vasculitis (defined by a compatible chest x-ray or computed tomography [CT] scan (diffuse pulmonary infiltrates), and
3.3. The absence of an alternative explanation for all pulmonary infiltrates (i.e. volume overload or pulmonary infection), and
3.4. At least one of the following:
3.4.1. Evidence of alveolar haemorrhage on bronchoscopic examination or increasingly bloody returns with bronchoalveolar lavage
3.4.2. Observed haemoptysis
3.4.3. Unexplained anaemia (less than 10 g/dl) or documented drop in haemoglobin (greater than 1 g/dl)
3.4.4. An increased diffusing capacity of carbon dioxide
4. Provision of informed consent by patient or a surrogate decision maker
5. Aged greater than or equal to 15 years, either sex

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
704

Key exclusion criteria
1. A diagnosis of vasculitis other than Wegener's granulomatosis or microscopic polyangiitis
2. Positive anti-glomerular basement membrane antibody test or renal biopsy demonstrating linear glomerular immunoglobulin deposition
3. Receipt of dialysis for greater than 21 days immediately prior to randomisation or prior renal transplant
4. Aged less than 15 years (aged less than 18 years at centres that do not treat paediatric patients)
5. Pregnancy
6. Treatment with greater than 1 intravenous (IV) dose of cyclophosphamide and/or greater than 14 days of oral cyclophosphamide and/or greater than 14 days of prednisone/prednisolone (greater than 30 mg/day) and/or greater than 1 dose of rituximab within the 28 days immediately prior to randomisation
7. A comorbidity that, in the opinion of the investigator, precludes the use of cyclophosphamide, glucocorticoids, or plasma exchange or absolutely mandates the use of plasma exchange

Added 30/10/2019:
8. Plasma exchange in 3 months prior to randomization

Date of first enrolment
30/09/2016

Date of final enrolment
31/07/2017

Locations

Countries of recruitment
United Kingdom

England

Australia

Canada

Czech Republic

Denmark

France

Germany

Italy

Mexico

Netherlands

New Zealand

Spain

Sweden

Switzerland

United States of America

Study participating centre
Addenbrooke's Hospital
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Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust (UK)

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Medical Research Council (MRC) (UK) (ref: 86772)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Food and Drug Administration (USA) and National Institutes of Health (USA) (ref: 1 R01 FD003516-01)

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	13/02/2020	14/02/2020	Yes	No
Results article		01/09/2022	27/09/2022	Yes	No
Protocol article	protocol	14/03/2013		Yes	No
HRA research summary			28/06/2023	No	No