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Rituximab versus cyclophosphamide in connective tissue disease-ILD

Submission date 01/04/2015	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 02/04/2015	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 10/05/2024	**Condition category** Respiratory	[_] Individual participant data

Plain English summary of protocol

Background and study aims
Interstitial lung disease (ILD), a condition that causes inflammation and scarring of the lungs, is the leading cause of death in systemic sclerosis (SSc), and a major cause of morbidity (or illness) in many other connective tissue diseases (CTDs) a group of conditions that are caused by over activity of the immune system. If connective tissue disease associated interstitial lung disease (CTD-ILD) is severe or progressive, immunosuppressive treatment (treatment used to damp down the immune system), such as intravenous cyclophosphamide, is required to suppress inflammation and minimise progressive lung scarring. Occasionally, even intensive standard immunosuppressive drugs fail to control lung inflammation, and progressive lung damage may develop that ultimately results in death. Rituximab, a novel immunosuppressive therapy, has been proven to be of benefit in suppressing inflammation associated with immune system over activity, including pulmonary inflammation in CTDs. In this study, we want to compare how well rituximab works compared to cyclophosphamide in treating patients with severe, progressive CTD-ILD.

Who can participate?
Adults diagnosed with CTD-ILD.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in group 1 are given rituximab on day one of the study and then on day 14. They are then given a placebo four weeks into the study for 16 weeks. Those in group 2 are given cyclophosphamide every 4 weeks from day one of the study to week 20. On day 14, they are given a placebo. Lung function for all participants is assessed at the end of the study.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Six NHS centres in the UK

When is the study starting and how long is it expected to run for?
November 2014 to January 2021 (updated 23/06/2021, previously: December 2020; updated 15 /08/2019, previously: August 2018)

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Veronica Tudor
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(updated 15/08/2019, previously: Dr Vicky Tsipouri)

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2012-003633-42

IRAS number

ClinicalTrials.gov number
NCT01862926

Secondary identifying numbers
17594

Study information

Scientific Title
A randomized, double blind controlled trial comparing rituximab against intravenous cyclophosphamide in connective tissue disease associated interstitial lung disease

Acronym
RECITAL

Study objectives
The aim of this trial is to we compare the effectiveness of rituximab against cyclophosphamide as first line therapy in patients with severe, progressive connective tissue disease associated interstitial lung disease (CTD-ILD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/LO/0968

Study design
Randomised; Interventional; Design type: Not specified, Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Interstitial lung disease in people with severe connective tissue disease, including systemic sclerosis, idiopathic interstitial myopathy (including polymyositis/dermatomyositis) and mixed connective tissue disease

Interventions
Patients will be randomised on a 1:1 ratio to intravenous rituximab or intravenous cyclophosphamide.
1. Rituximab group: Rituximab will be given at a dose of 1000 mg at day 0 and day 14. At week 4 through to week 20 patients will receive placebo.
2. Cyclophosphamide group: Cyclophosphamide will be given at a dose of 600 mg/m2 body surface area every 4 weeks from day 0 through to week 20. At day 14 the group will receive placebo.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Rituximab, cyclophosphamide

Primary outcome measure
Change in forced vital capacity (FVC) at 24 weeks

Secondary outcome measures
Safety, change in diffusing capacity for carbon monoxide (DLco)

Overall study start date
03/11/2014

Completion date
12/01/2021

Eligibility

Key inclusion criteria
Subjects will be recruited prospectively from rheumatology or interstitial lung disease units at 6 UK centres.

1. A diagnosis of connective tissue disease, based on internationally accepted criteria, in one of the following categories:
1.1. Systemic sclerosis
1.2. Idiopathic interstitial myopathy (including polymyositis/dermatomyositis)
1.3. Mixed connective tissue disease
2. Severe and/or progressive interstitial lung disease associated with the underlying connective tissue disease.
3. Chest HRCT performed within 12 months of randomisation
4. Intention of the caring physician to treat the ILD with intravenous cyclophosphamide (with treatment indications including deteriorating symptoms attributable to ILD, deteriorating lung function tests, worsening gas exchange or extent of ILD at first presentation)and where there is a reasonable expectation that immunosuppressive treatment will stabilize or improve CTD-ILD
5. Written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 116; UK Sample Size: 116

Total final enrolment
104

Key exclusion criteria
1. Age <18 or >80 years.
2. Previous treatment with rituximab and/or intravenous cyclophosphamide
3. Known hypersensitivity to rituximab or cyclophosphamide or their components
4. Significant (in the opinion of the investigator) other organ co-morbidity including cardiac, hepatic or renal impairment
5, Co-existent obstructive pulmonary disease (e.g. asthma, COPD, emphysema) with pre bronchodilator FEV1/FVC <70%
6, Patients at significant risk for infectious complications following immunosuppression including HIV positive or other immunodeficiency syndromes (including hypogammaglobulineamia)
7. Suspected or proven untreated tuberculosis
8. Viral hepatitis
9. Infection requiring antibiotic treatment in the preceding four weeks
10. Unexplained neurological symptoms (which may be suggestive of progressive mutifocal leukoencephalopathy; PML).
11. Other investigational therapy (participation in research trial) received within 8 weeks of randomisation
12. Immunosuppressive or CTD disease modifying therapy (other than corticosteroids) received within 2 weeks of randomisation
13. Pregnant or breast feeding women, or women of child-bearing potential, not using a reliable contraceptive method for up to 12 months following IMP
14. Unexplained haematuria, or previous bladder carcinoma
15. CT scan > 12 months from randomisation
16. Unable to provide informed written consent

Date of first enrolment
03/11/2014

Date of final enrolment
31/05/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Brompton & Harefield NHS Foundation Trust
Sydney Street
London
United Kingdom
SW3 6NP

Sponsor information

Organisation
Royal Brompton & Harefield NHS trust

Sponsor details
Royal Brompton Hospital
Sydney Street
London
England
United Kingdom
SW3 6NP

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02218z997

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/11/2022

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	15/06/2017	23/07/2019	Yes	No
Results article		11/11/2022	14/11/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/02/2024	10/05/2024	Yes	No