

# Rituximab versus cyclophosphamide in connective tissue disease-ILD

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|----------------------------------------|---------------------------------------------------|---------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>01/04/2015   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input checked="" type="checkbox"/> Protocol |
| <b>Registration date</b><br>02/04/2015 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>10/05/2024       | <b>Condition category</b><br>Respiratory          | <input type="checkbox"/> 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

**ClinicalTrials.gov (NCT)**  
NCT01862926

**Clinical Trials Information System (CTIS)**  
2012-003633-42

**Protocol serial number**  
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

### **Primary study design**

Interventional

### **Study design**

Randomised; Interventional; Design type: Not specified, Treatment

### **Study type(s)**

Treatment

### **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/m<sup>2</sup> 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(s)**

Change in forced vital capacity (FVC) at 24 weeks

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

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

### **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

## Healthy volunteers allowed

No

## Age group

Adult

## Sex

All

## 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 hypogammaglobulinaemia)
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 multifocal

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**

United Kingdom

England

**Study participating centre**

**Royal Brompton & Harefield NHS Foundation Trust**

Sydney Street

London

United Kingdom

SW3 6NP

## **Sponsor information**

**Organisation**

Royal Brompton & Harefield NHS trust

**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

**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? |
|--------------------------------------|----------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a>      |          | 11/11/2022   | 14/11/2022 | Yes            | No              |
| <a href="#">Results article</a>      |          | 01/02/2024   | 10/05/2024 | Yes            | No              |
| <a href="#">Protocol article</a>     | protocol | 15/06/2017   | 23/07/2019 | Yes            | No              |
| <a href="#">HRA research summary</a> |          |              | 28/06/2023 | No             | No              |