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Study of co-trimoxazole in advanced pulmonary fibrosis

Submission date	Recruitment status	[_] Prospectively registered
20/08/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
09/10/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
01/11/2021	Respiratory	

Plain English summary of protocol

Background and study aims
Pulmonary fibrosis is a disease in which scars form in the lung tissues, leading to serious breathing problems such as perpetual shortness of breath. Previous studies have shown clinical improvement in patients treated with the drug co-trimoxazole. The aim of this study is to expand a previous small study to a larger study and confirm whether co-trimoxazole is effective at treating pulmonary fibrosis.

Who can participate?
Patients aged 40 to 86 with pulmonary fibrosis.

What does the study involve?
Participants are randomly allocated to be treated with either co-trimoxazole or an identical placebo (dummy drug) for 12 weeks. Participants are assessed with walking tests, lung function tests, questionnaires and blood tests.

What are the possible benefits and risks of participating?
The risks are minimal and the safety of cotrimoxazole is well established in transplant cases and other immune-suppressed patients, where it is used long-term. The study excludes those allergic to cotrimoxazole (septrin) and requires patients to take folic acid for bone marrow protection. The study is short (12 weeks) and placebo patients can receive active treatment after that so they are not denied active treatment for long.

Where is the study run from?
St Helier Hospital (UK)

When is the study starting and how long is it expected to run for?
September 2012 to October 2021

Who is funding the study?
Peel Medical Trust Fund, Rotary Club and the Morriston-Davies Trust (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2006-004927-12

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
06-09-2006-0208-296-2401

Study information

Scientific Title
A double-blind, randomised, placebo-controlled study of co-trimoxazole in advanced pulmonary fibrosis

Study objectives
Cotrimoxazole may have therapeutic benefit pulmonary fibrosis (both UIP/IPF and Fibrotic NSIP)

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Research Ethics Committee, 15/08/2007, ref: 07/MRE01/36

Study design
Double-blind randomised placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Advanced pulmonary fibrosis (UIP/IPF and fibrotic NSIP)

Interventions
The study will consist of two phases:
1. Double-blind randomised phase (3 months)
2. Open-label extension phase (to complete 12 months on treatment)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Co-trimoxazole

Primary outcome(s)
Change from baseline to 3 months in forced vital capacity

Key secondary outcome(s))
Change from baseline to 3 months in:
1. Shuttle walking test
2. Symptom score on the MRC 5-Point Dyspnoea Scale.
3. Total lung capacity
4. Pulmonary gas exchange, as measured by DLCO and KCO
5. Cough, as measured by diary cards
6. SGRQ
7. Resting oxygen saturation on air
8. Chest radiograph
9. Changes in pulmonary cytokines relevant to this disease at entry & 3 months

A further efficacy endpoint will be a formal assessment of response to therapy (Favourable Response, Stable Response, Failure of Response) as defined in the ATS/ERS International Consensus statement (2000).

Completion date
01/10/2021

Eligibility

Key inclusion criteria
1. Male or female
2. Aged 40 86 years
3. An established clinical history consistent with IIP according to the criteria for diagnosis outlined in the ATS/ERS consensus statement. (Bronchoscopic and/or biopsy data, although desirable, are not required for patient entry into the trial)
4. Clear cut HRCT evidence of UIP or fibrotic NSIP. An HRCT within 6 months of study enrolment is required. Lung function within 3 months of enrolement
5. Permitted concurrent therapies are:
5.1. Prednisolone 1 30 mg per day, established for at least 3 months at study entry
5.2. Short burst oxygen therapy for symptomatic benefit only
6. Stability of the disease process itself following the introduction of prednisolone is not required for study entry
7. Patients in whom oral steroids have been withdrawn due to lack of efficacy are eligible
8. Oxygen desaturation below 90% on a shuttle-walking test
9. MRC score of 3 or more

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. A secondary cause for pulmonary fibrosis
2. Subject currently smokes
3. A recognized coexisting respiratory disorder (e.g. significant COPD, asthma, sarcoid or lung carcinoma) that in the opinion of the investigator would put the patient at risk or invalidate the study outcome measures
4. A requirement for long-term oxygen therapy (LTOT) at entry as defined by the prescription of oxygen to be used for greater than or equal to 12 hours therapy per day
5. Overt and persistent right heart failure
6. Inability to perform the shuttle walking tests
7. Women who are pregnant, or who have the potential to become pregnant during the course of the study, or who are breast feeding
8. Co-trimoxazole allergy or prior known intolerance
9. Untreated vitamin B12 deficiency
10. Suspected or known glucose-6-phosphate dehydrogenase deficiency
11. Impaired renal function with an established creatinine greater than 175 ìmol/l
12. The following therapies will not be permitted on entry to the study:
12.1. Long-term oxygen therapy (LTOT)
12.2. Azathioprine
12.3 Cyclophosphamide
12.4. Methotrexate
12.5. D-penicillamine

12.6. Colchicine
12.7. Gamma-interferon
13. The following therapies will require caution or increased monitoring:
13.1. Digoxin
13.2 Warfarin
13.3. Phenytoin
13.4. Sulphonylureas
13.5. Procainamide hydrochloride

Date of first enrolment
06/10/2012

Date of final enrolment
06/10/2020

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Helier Hospital
surrey
United Kingdom
SM51AA

Sponsor information

Organisation
St Helier Hospital (UK)

ROR
https://ror.org/019hb9542

Funder(s)

Funder type
Charity

Funder Name

Peel Medical Trust Fund (UK)

Funder Name
Rotary Club Banstead, Surrey (UK)

Funder Name
Morriston Davies Joint Fellowship (UK)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication as it is a double-blind study, although I plan to publish the first 50 cases from their out of study data (treatment out of study in the open part of the study to show how steady the lung function has remained).

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Abstract results	results	16/11/2016	24/01/2020	No	No