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Treating interstitial pneumonia with the addition of co-trimoxazole

Submission date 06/10/2007	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 31/10/2007	**Overall study status** Completed	
Last Edited 15/03/2016	**Condition category** Respiratory	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
N/A

Study information

Scientific Title
Treating Interstitial Pneumonia with the Addition of Co-trimoxazole

Acronym
TIPAC

Study objectives
Idiopathic Pulmonary Fibrosis (IPF) is a condition that results in uniformly progressive deterioration in exercise capacity with increasing breathlessness. The majority of patients die from respiratory failure within 3 years of diagnosis. The cause is unknown, there is no cure and no medical treatment changes the life expectancy. However, in a small pilot study of 20 patients, high dose oral co-trimoxazole has been shown to have remarkable results in terms of pulmonary function and exercise capacity. We expect that the results of the pilot study will be translated into significant patient benefit when co-trimoxazole is evaluated in a placebo-controlled fashion in the current larger study.

Primary aim:
To determine the benefits and adverse effects of treating patients with idiopathic pulmonary fibrosis with co-trimoxazole 960 mg twice daily for 12 months in addition to standard therapy with prednisolone when compared to placebo.

Secondary aim:
To determine the cost effectiveness of this therapy from the viewpoint of the National Health Service.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Cambridgeshire 4 Research Ethics Committee, 04/09/2007, ref: 07/MRE05/45

Study design
Double-blind, placebo-controlled, randomised multicentre study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Idiopathic pulmonary fibrosis (IPF)

Interventions
Patients will be randomised to the following two groups:

1. Intervention group: Co-trimoxazole (non-proprietary) 960 mg (as 2 tablets of 480 mg) twice daily plus folic acid (non-proprietary) 5 mg orally once daily.
2. Control group: Placebo (manufactured by pharmacy at Guy's and St Thomas's Hospital, to be identical in appearance to co-trimoxazole 480 mg) 2 tablets twice daily plus folic acid (non-proprietary) 5 mg orally once daily.

Duration of intervention: 12 months

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
1. Co-trimoxazole 2. Prednisolone

Primary outcome(s)
Change in forced vital capacity after 12 months of study drug.

Key secondary outcome(s))
1. Change in the Medical Research Council (MRC) breathlessness score, assessed at baseline, 6 weeks, 6, 9 and 12 months in all participants
2. Change in total lung capacity, assessed at baseline, 6 and 12 months in all participants
3. Change in total lung diffusing capacity of carbon monoxide, assessed at baseline, 6 and 12 months in a subgroup of participants
4. Change in St Georges Respiratory Questionnaire, assessed at baseline, 6 and 12 months in all participants
5. Change in 6 minute walking distance and desaturation, assessed at baseline, 6 and 12 months in a subgroup of participants
6. Change in EuroQol (EQ-5D) score, assessed at baseline, 6 weeks, 6, 9 and 12 months in all participants
7. Prednisolone dose at 12 months
8. Healthcare utilisation (including hospitalisation, primary care contacts and therapy) over 12 months
9. Adverse events, recorded throughout the trial

Completion date
31/10/2009

Eligibility

Key inclusion criteria
1. Male or female, aged greater than 40 years
2. Female subjects must be of non-childbearing potential, defined as follows:
2.1. Postmenopausal females who have had at least 12 months of spontaneous amenorrhoea or 6 months of spontaneous amenorrhoea with serum Follicle Stimulating Hormone (FSH) greater than 40 mIU/ml
2.2. Females who have had a hysterectomy or bilateral oophorectomy for at least 6 weeks
3. Able to provide informed consent
4. A clinical labelled diagnosis of fibrotic idiopathic interstitial pneumonia with High Resolution Computed Tomography (HRCT) scan features compatible with Usual Interstitial Pneumonia (UIP) or fibrotic Non-Specific Interstitial Pneumonia (NSIP). The following criteria adapted from the American Thoracic Society/European Respiratory Society (ATS/ERS) consensus statement will be used for the diagnosis of the clinical manifestation of UIP (idiopathic pulmonary fibrosis):
4.1. Major criteria (all present):
4.1.1. Exclusion of other known causes of interstitial lung disease, such as drug toxicities, environmental exposures, and collagen vascular diseases
4.1.2. Abnormal pulmonary function studies that include evidence of restriction with or without impaired gas exchange
4.1.3. Bibasal reticular abnormalities with minimal ground glass opacities on HRCT
4.2. Minor criteria (two out of three features):

4.2.1. Insidious onset of otherwise unexplained dyspnoea on exertion
4.2.2. Duration of illness 3 months
4.2.3. Bibasal inspiratory crackles (dry or 'Velcro-' type in quality)

Note: Patients with clinical diagnosis of non-specific interstitial pneumonia will be entered if fibrotic features are predominant on HRCT. Histology will not be required as an entry criterion however histology from lung biopsy or autopsy will be reviewed if available.

5. Patients will have had initial treatment of prednisolone +/- azathioprine, as indicated and described in the current British Thoracic Society (BTS) guidelines, without a significant response to immunosuppressive therapy that would make the physician doubt the diagnosis of fibrotic idiopathic interstitial pneumonia
6. Patients should be on stable treatment regimen for at least 6 weeks. Patients may be on no immunosuppressive medication or may be receiving immunosuppressive medication in the form of oral prednisolone up to a dose of 20 mg per day +/- azathioprine. Patients receiving higher doses of up to 0.5 mg/kg may be enrolled in exceptional circumstances after discussion with the principal investigator
7. Medical Research Council (MRC) dyspnoea score of greater than or equal to 2
8. A normal serum folate and B12 (to ensure no bone marrow or neurological adverse effects occur with folate therapy in B12 deficient individuals) is required at screening
9. Subjects have a 12-lead Electrocardiogram (ECG) recording that does not demonstrate any clinically important abnormality that, in the opinion of the investigator, would make the subject unsuitable for participation in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. A secondary cause for pulmonary fibrosis including a diagnosis of asbestosis, drug induced pulmonary fibrosis, collagen vascular disease or other secondary pulmonary fibrosis
2. A recognised significant co-existing respiratory disorder
3. Long-term oxygen therapy
4. Receiving anti-oxidant therapy including acetylcysteine within the last 6 weeks
5. A respiratory tract infection within the last 2 months
6. Overt and persistent heart failure, a myocardial infarction within 3 years, ischaemic heart disease requiring more than one regular therapy or a clinically significant uncontrolled arrhythmia (including Mobitz type II or third degree heart block)
7. Significant medical, surgical or psychiatric disease that in the opinion of the patients' attending physician would affect subject safety or influence the study outcome
8. Women who are pregnant or breast-feeding
9. Patients receiving immunosuppressant medication (with the exception of prednisolone and azathioprine according to guidelines)

10. Co-trimoxazole allergy or intolerance and patients receiving medication known to interact with co-trimoxazole
11. Untreated folate or B12 deficiency
12. Glucose-6-phosphate dehydrogenase deficiency as measured at screening (in males only)
13. Receipt of an investigational drug or biological agent within the 4 weeks prior to entry into this study
14. Patients with evidence of drug or alcohol misuse

Date of first enrolment
01/11/2007

Date of final enrolment
31/10/2009

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of East Anglia
Norwich
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Sponsor information

Organisation
University of East Anglia (UK)

ROR
https://ror.org/026k5mg93

Funder(s)

Funder type
Government

Funder Name
East Anglian Thoracic Society Sponshorship (UK)

Funder Name
National Institute for Health Research (UK) - Research for Patient Benefit Program (ref: PB-PG-0906-11116)

Results and Publications

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	01/02/2013		Yes	No