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Testing oral corticosteroids versus placebo for the treatment of fibrotic hypersensitivity pneumonitis

Submission date 06/12/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 28/02/2025	**Overall study status** Ongoing	
Last Edited 12/02/2026	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Fibrotic hypersensitivity pneumonitis (FHP) is a devastating lung disease which results in scarring of the lungs. As the scarring worsens, patients struggle to breathe. They can develop a harsh, hacking cough, lose a lot of weight, have a deteriorating quality of life and may become housebound. Life expectancy after diagnosis is only 5 years on average. FHP is estimated to affect 3 people per 100,000 but it is more common in those over 65 years (about 11 people per 100,000); there are around 2000 new cases per year in the UK. FHP is unusual because the lungs have both thickening (inflammation) and scarring (fibrosis). This combination makes FHP much more complicated to treat. Treatments and care for people with FHP vary widely across the UK and the world. The aim of this study is to determine whether steroids (prednisolone) are beneficial for people with FHP.

Who can participate?
Patients aged 18 years and over with recently diagnosed FHP

What does the study involve?
Participants will be allocated at random (like tossing a coin) to receive either oral steroid tablets or placebo tablets (which look identical). They will take the steroids or placebo for 6 months. The researchers will prescribe the steroid doses that doctors regularly use, and all participants will continue with any treatments they are taking for other reasons (such as blood pressure medication). The potential benefit of the steroids will be measured using lung function tests at the start and after 3 and 6 months of treatment. These are reliable tests used in day-to-day clinical care. Participants will fill out questionnaires about their symptoms: breathlessness; cough; and quality of life. The researchers will monitor for any side effects of steroids. They will also investigate whether steroids offer value for money to the NHS and wider care services. The study will provide much-needed evidence for guiding treatment and improving clinical care for FHP patients.

What are the possible benefits and risks of participating?
Prednisolone is commonly used to treat fibrotic hypersensitivity pneumonitis. The Participant

Information Sheet (PIS) outlines the key side effects for participants. As part of the consent conversation, the site team will discuss possible side effects with the participant and answer any questions. Due to the precautions outlined in the Summary of Product Characteristics (SmPC), potential participants with contraindications to prednisolone will be excluded from the trial. Patients with known but controlled diabetes have been advised to closely monitor their blood sugar levels as prednisolone can increase blood sugar levels. A full assessment of these risks is outlined in the trial protocol (section 2.1) and the site teams will be trained in assessing these risks during recruitment.
The risk versus benefit to participants of being on the placebo IMP is unknown as such a trial has not been conducted in this population previously. This trial aims to answer that question. Participants allocated to receive placebo could be at risk of disease progression, but it is not known if the risk is any higher than in the prednisolone group. The main benefit of taking part is to potentially help improve the healthcare of people with FHP in the future.

Where is the study run from?
University of Exeter (UK)

When is the study starting and how long is it expected to run for?
June 2024 to May 2028

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

Who is the main contact?
Miss Lucy Tregellas, chorus@exeter.ac.uk

Contact information

Type(s)
Scientific

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Miss Lucy Tregellas

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Type(s)
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1010739

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
2409609, CPMS 66336

Study information

Scientific Title
CHORUS: a multi-centre double-blind randomised placebo-controlled group-sequential superiority trial to assess the effectiveness and cost-effectiveness of oral Corticosteroids in patients witH fibrOtic hypeRsensitivity pneUmonitiS

Acronym
CHORUS

Study objectives
Primary objective:
To assess the effectiveness of 26 weeks of treatment with prednisolone vs placebo on disease progression, as measured by the pulmonary function test, forced vital capacity (FVC).

Secondary objectives:
1. Assess effectiveness of prednisolone vs placebo on disease progression at 12 weeks post-randomisation on FVC
2. Assess effectiveness of prednisolone vs placebo on disease progression at 26 weeks post-randomisation on (a) FVC, (b) Diffusion Co-efficient for carbon monoxide (DLco)
3. Assess initiation of antifibrotic therapy and/or additional immunosuppressive therapy during the 26-week treatment period
4. Assess effect of prednisolone vs placebo on participant-reported outcome measures (PROMs) of quality of life, including disease-specific quality of life measures, at baseline, week 12 and week 26 post-randomisation
5. Assess safety of prednisolone
6. Assess health/social care service resource use
7. Assess cost-effectiveness of prednisolone vs placebo over 26 weeks of treatment

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 18/02/2025, London - Dulwich Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048276; dulwich.rec@hra.nhs.uk), ref: 25/LO/0018

Study design
Randomized double-blind placebo-controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Fibrotic hypersensitivity pneumonitis

Interventions
Participants will be randomised into the trial by a delegated member of the site team using an online randomisation service. Trial participants will be randomised on a 1:1 ratio to receive either 26 weeks prednisolone or 26 weeks placebo.

For blinding purposes, the active drug will be over-encapsulated. Placebo capsules will be manufactured to match in appearance but will not contain any active ingredients.

Participants will start on a dose of 40 mg (or matched placebo capsules) which will be gradually reduced over 12 weeks to a 10 mg maintenance dose which will be taken for 14 weeks. This will be followed by a 9-week IMP weaning period.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Prednisolone

Primary outcome(s)
Absolute FVC, measured in millilitres (ml), will be recorded using the pulmonary function test (PFT), at 26 weeks post-randomisation. The primary outcome is the change in absolute FVC between baseline and 26 weeks post-randomisation.

Key secondary outcome(s))
1. Absolute FVC, measured in millilitres (ml) will be recorded using the pulmonary function test (PFT) at 12 weeks post-randomisation and used to calculate change in absolute FVC between baseline and 12 weeks post-randomisation
2. Percentage change in FVC will be calculated (using the absolute FVC values collected at baseline, 12 and 26 weeks post-randomisation) between (i) baseline and 12 weeks and (ii) baseline and 26 weeks post-randomisation

3. Absolute change in percentage predicted FVC will be calculated between (i) baseline and 12 weeks and (ii) baseline and 26 weeks post-randomisation, using percentage predicted FVC calculated centrally by ExeCTU using Global Lung Initiative (GLI) reference equation
4. Absolute DLco, measured in mmol min-1 kPa-1 , will be recorded using the European Respiratory Society (ERS) guidelines, at baseline and 26 weeks post-randomisation and used to calculate change in absolute DLCO between baseline and 26 weeks post-randomisation
5. Percentage change in DLco will be calculated (using the absolute DLco values collected at baseline and 26 weeks post-randomisation) between baseline and 26 weeks post-randomisation
6. Absolute change in percentage predicted DLco will be calculated between baseline and 26 weeks post-randomisation.
7. Initiation of antifibrotic therapy given by 26 weeks post-randomisation as reported on additional therapies eCRF
8. Additional immunosuppressant therapy given by 26 weeks post-randomisation as reported on additional therapies eCRF
9. Quality of life will be measured at baseline, 12 and 26 weeks post-randomisation. Changes in quality of life from (i) baseline to week 12 and (ii) baseline to week 26 will be measured using patient-reported outcome measures (PROMs):
9.1. L-PF questionnaire (dyspnoea, cough and fatigue domain scores of principal interest)
9.2. PGI-S scale
9.3. The cough VAS
9.4. EQ-5D-5L – Visual Analogue Scale
10. Safety data will be collected in accordance with MedDRA and defined as the number and proportion of participants experiencing Serious Adverse Events (SAEs) and related Adverse Events (AEs) throughout the duration of the trial
11. Health/social care resource use will be assessed using a participant report Resource Use Questionnaire at baseline and 12 and 26 weeks post-randomisation
12. Cost-effectiveness will be assessed via EQ-5D-5L and Resource Use Questionnaire data collected at baseline, 12 and 26 weeks post randomisation

Measured at baseline, 12 weeks and week 26 post-randomisation

Completion date
31/05/2028

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. ILD multi-disciplinary diagnosis of FHP within the last 6 months
3. % predicted FVC ≥40% at baseline (as per GLI equation)
4. % predicted DLCO ≥25% at baseline
5. FEV1/FVC ratio ≥0.7 at baseline
6. >10% fibrosis on CT taken as standard of care for the MDT diagnosis
7. Able to provide informed consent
8. People of child-bearing potential must be willing to:
8.1. Take a pregnancy test at baseline, before randomisation
8.2. Use of a highly effective method of contraception for the duration of the trial (35 weeks)
8.3. Inform the research clinical team if pregnancy occurs during trial participation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
110 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Previous or current therapy with prednisolone or other immunosuppressive agent for FHP
2. Active infection (use of antibiotics must be completed 2 weeks prior to the baseline visit. Prophylactic antibiotics are allowed)
3. Emphysema>fibrosis on CT scan
4. BMI>44 kg/m2
5. Currently enrolled in another investigational drug trial
6. Non-respiratory conditions requiring use of immunosuppressive therapy (including prednisolone)
7. Any condition that might be significantly exacerbated by the administration of prednisolone, including but not limited to: Cushing's and Conn's Syndromes, Addison's disease, poorly controlled/difficult to control diabetes
8. Patients with underlying liver cirrhosis (Child Pugh, B, or C hepatic impairment).
9. Stage 4/5 chronic kidney disease (eGFR <30 ml/min/1.73 m2)
10. Patients with unstable cardiac disease or a significant disease or condition other than the ILD under trial, which in the opinion of the investigator, may put the patient at risk because of participation, interfere with trial procedures, or cause concern regarding the patient's ability to participate in the trial
11. Use of potent inducers of prednisolone including phenytoin, rifabutin, carbamazepine, ketoconazole, rifamycins. Please refer to the Summary of Product Characteristics
12. Patients with ocular herpes simplex
13. Known allergy to prednisolone or its excipients including lactose anhydrous or capsule ingredients hydroxypropylmethylcellulose, water, dye – copper complex of chlorophyllins E141ii
14. Pregnant, breastfeeding, or planning to conceive in the next 35 weeks

Date of first enrolment
01/05/2025

Date of final enrolment
31/03/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Devon University Healthcare NHS Foundation Trust
Royal Devon University NHS Ft
Barrack Road
Exeter
England
EX2 5DW

Study participating centre
Royal Brompton Hospital
Sydney Street
London
England
SW3 6NP

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Lane
Colney
Norwich
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NR4 7UY

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
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NE7 7DN

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road

Westbury-on-trym
Bristol
England
BS10 5NB

Study participating centre
NHS Tayside
Kings Croos
Clepington Road
Dundee
Scotland
DD3 8EA

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
University Hospitals of Morecambe Bay NHS Foundation Trust
Westmorland General Hospital
Burton Road
Kendal
England
LA9 7RG

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London

England
NW1 2PG

Study participating centre
Guys & St Thomas Foundation Trust
Great Maze Pond
London
England
SE1 9RT

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
England
M23 9LT

Study participating centre
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
England
WV10 0QP

Study participating centre
Musgrove Park Hospital
Musgrove Park
Taunton
England
TA1 5DA

Study participating centre
Castle Hill Hospital
Entrance 3
Castle Road
Cottingham
England
HU16 5JQ

Study participating centre
Princess Alexandra Hospital
Hamstel Road
Harlow
England
CM20 1QX

Study participating centre
Liverpool University Hospital (Aintree site)
Aintree University Hospital, Lower Lane
Liverpool, Merseyside
England
L9 7AL

Sponsor information

Organisation
University of Exeter

ROR
https://ror.org/03yghzc09

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

Results and Publications

Individual participant data (IPD) sharing plan
Anonymised research data and outputs will be stored in a research repository hosted by one of the collaborating organisations (Sponsor and/or University of Exeter) to facilitate access to, and the impact of the research. All future research proposals must obtain the appropriate ethical and regulatory approvals.

IPD sharing plan summary
Stored in publicly available repository