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Studying acute exacerbations and response: the COPD STARR 2 study

Submission date
14/08/2017

Recruitment status
No longer recruiting

Registration date
23/08/2017

Overall study status
Completed

Last Edited
02/11/2022

Condition category
Respiratory

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) affects adults and is largely caused by smoking cigarettes. It is predicted to be the 3rd leading cause of death by 2020 affecting over 250 million people worldwide. COPD makes breathing increasingly difficult, with frequent periods of worsening symptoms. These are termed exacerbations and current treatment strategies rely on oral corticosteroids (prednisolone) and antibiotics but this is in a "one size fits all" approach. There is little evidence supporting this strategy and both treatments can potentially cause harm. In addition to this, previous findings have shown that eosinophil (white blood cell) counts within blood samples from COPD patients can be used as a marker to determine treatment with oral steroids. The aim of this study is to find out whether personalising treatment based on eosinophil counts is superior to current standard treatment strategies.

Who can participate?
Patients aged 40 or over with COPD

What does the study involve?
A participant's involvement lasts up to 12 months and involves up to 5 visits. These visits involve completing questionnaires, undergoing breathing tests, and giving urine and blood samples. Participants take the study drugs for 14 days during an exacerbation, when they are randomly allocated to one of two groups. One group receives antibiotics and either prednisolone or placebo depending on their blood eosinophil count. The other group receives prednisolone and antibiotics regardless of their blood eosinophil count. Participants are followed up at days 14, 30, 90 with a medical review of notes at 12 months. Participants may be re-randomised and followed up if they have further exacerbations after the 30 day visit. The number of participants who need more treatment, hospitalisation or die is assessed.

What are the possible benefits and risks of participating?
Participants receive no direct benefit from being involved in the study. However, the information from this study may be used to improve the treatment of people with COPD in the future. The breathing tests may cause coughing, chest tightness and occasional wheezing. The

blood samples may cause some mild discomfort but this is expected to stop very quickly. Antibiotics can cause side effects such as stomach upset or rash. On very rare occasions, the participant may be allergic to prednisolone, antibiotics or the placebo.

Where is the study run from?
1. Bicester Health Centre (UK)
2. Broadshires Health Centre (UK)
3. Montgomery House Surgery (UK)
4. White Horse Medical Practice (UK)
5. Eynsham Medical Centre (UK)
6. Windrush Medical Practice (UK)
7. Gladstone Surgery (UK)
8. Alchester Medical Group (UK)
9. Woodlands Medical Centre (UK)
10. Haddenham Medical Centre (UK)
11. Morland House Surgery (UK)
12. Norden House (UK)
13. Swan Practice (UK)
14. Whitchurch Surgery (UK)

When is the study starting and how long is it expected to run for?
November 2012 to October 2020

Who is funding the study?
NIHR Trainees Co-ordinating Centre (UK)

Who is the main contact?
Professor Mona Bafadhel, mona.bafadhel@ndm.ox.ac.uk

Contact information

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Public

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Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2017-001586-24

ClinicalTrials.gov (NCT)
NCT04458636

Protocol serial number
34829

Study information

Scientific Title
Delivering personalised care in the management of exacerbations of chronic obstructive pulmonary disease: a multi-centre randomised clinical trial

Acronym
COPD STARR 2

Study objectives
Chronic obstructive pulmonary disease (COPD) affects adults and is largely caused by cigarette smoke in the developed world. It is predicted to be the 3rd leading cause of death by 2020 affecting over 250 million people worldwide. COPD is characterised by progressive airflow obstruction punctuated by frequent periods of worsening in respiratory symptoms and function associated with a significant impact on quality of life. These episodes are termed exacerbations and current treatment strategies rely on oral corticosteroids (prednisolone) and antibiotics but this is in a "one size fits all" approach. However, there is little evidence supporting this strategy and both treatments can potentially cause harm. In addition to this, previous findings have shown that eosinophil counts within blood samples from COPD patients can be used as a biomarker to determine treatment with oral steroids. The study hypothesis is that personalising this treatment approach during an exacerbation of COPD, to direct whether corticosteroids is necessary for all patients, depending on the results of the eosinophil count from near-patient testing, is superior to current standard treatment strategies in the primary care setting.

Ethics approval required
Old ethics approval format

Ethics approval(s)

London – Fulham Research Ethics Committee, 04/08/2017, ref: 17/LO/1135

Study design
Randomised; Interventional; Design type: Treatment, Drug, Management of Care

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease

Interventions
Current interventions as of 29/01/2020
STARR 2 will be recruiting 228 participants with COPD from GP surgeries within the Thames Valley and South Midlands. A participant's involvement will last up until 12 months and will involve up to 5 visits. These visits will consist of CRF completion, questionnaires, breathing tests, urine testing, blood samples and spirometry. Participants will only be taking the trial drugs for 14 days during an exacerbation.
Consented participants will be randomised (1:1) to standard or directed therapy using the centralised computer randomisation service RRAMP (https://rramp.octru.ox.ac.uk) provided by the Oxford Clinical Trials Research Unit (OCTRU). Randomisation will be undertaken using stratification to ensure a balanced allocation across treatment groups, stratified by eosinophil count, disease severity as measured by FEV at baseline and prior exacerbation history.
As patients with COPD commonly experience on average two exacerbations per year, participants can be re-randomised if they experience a further exacerbation which meets the eligibility criteria and they consent to continue. This re-randomisation can occur in participants who have completed the study (attended a Day 90 visit), or participants who have completed a Day 30 visit. A maximum of 4 exacerbations per participant can be randomised to the study arms.
All participants will be blinded to prednisolone therapy and receive open-labelled antibiotics (doxycycline 100mg once per day for 7 days). Participants in the ‘blood eosinophil directed’ study arm will receive antibiotic (doxycycline, open labelled) and IMP (prednisolone or placebo) dependent on the blood eosinophil count at the randomisation (exacerbation visit). Participants in the ‘standard therapy’ study arm will receive IMP (prednisolone) and antibiotic (doxycycline, open labelled) irrespective of the blood eosinophil count at randomisation.
Prednisolone therapy consists of prednisolone 30mg tablet taken orally per day for 14 days.
Participants are followed up at days 14, 30, 90 with a medical review of notes at 12 months.

Previous interventions
STARR 2 will be recruiting 228 participants with COPD from GP surgeries within the Thames Valley and South Midlands. A participant's involvement will last up until 12 months and will involve up to 5 visits. These visits will consist of CRF completion, questionnaires, breathing tests, urine testing, blood samples and spirometry. Participants will only be taking the trial drugs for 14 days during an exacerbation.

Consented participants will be randomised (1:1) to standard or directed therapy using the centralised computer randomisation service RRAMP (https://rramp.octru.ox.ac.uk) provided by

the Oxford Clinical Trials Research Unit (OCTRU). Randomisation will be undertaken using stratification to ensure a balanced allocation across treatment groups, stratified by eosinophil count, disease severity as measured by FEV at baseline and prior exacerbation history.

All participants will be blinded to prednisolone therapy and receive open-labelled antibiotics (doxycycline 100mg once per day for 7 days). Participants in the 'blood eosinophil directed' study arm will receive antibiotic (doxycycline, open labelled) and IMP (prednisolone or placebo) dependent on the blood eosinophil count at the randomisation (exacerbation visit). Participants in the 'standard therapy' study arm will receive IMP (prednisolone) and antibiotic (doxycycline, open labelled) irrespective of the blood eosinophil count at randomisation.

Prednisolone therapy consists of prednisolone 30mg tablet taken orally per day for 14 days. Participants are followed up at days 14, 30, 90 with a medical review of notes at 12 months.

Intervention Type
Other

Phase
Phase IV

Primary outcome(s)
Efficacy of blood-eosinophil directed corticosteroid therapy compared to standard care measured by looking at the frequency of participants needing re-treatment, hospitalisation, death at 30 and 90 days

Key secondary outcome(s))
Measured at baseline, day 14, 30 and 90:
1. Quality of life, measured using CAT and EQ-5D
2. Symptoms, measured using VAS
3. Lung function, measured using FEV1
3. Healthcare utilisation, measured using exacerbation frequency in 12 months

Exploratory outcome measures:
1. Stability of blood eosinophils, measured by the change in blood eosinophil counts at all visits (except 12 months)
2. Stability of mediatory levels in the blood, measured by looking at the change in inflammatory mediators during a stable state and at exacerbation

Completion date
09/10/2020

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the trial
2. Male or female, aged 40 years or above
3. Diagnosed with COPD (primary or secondary care diagnosis) with spirometric confirmation of airflow obstruction (FEV1/FVC ratio <0.7)
4. A history of at least 1 exacerbation in the previous 12 months, requiring systemic

corticosteroids and/or antibiotics
5. Current or ex-smoker with at least a 10 pack year smoking history
6. In the opinion of the research staff, is able and willing to comply with all trial requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
308

Key exclusion criteria
1. History of atopic childhood asthma
2. Current history of primary lung malignancy or current active pulmonary TB
3. Clinically relevant disease or disorder (past or present) which in the opinion of the investigator may either put the subject at risk because of participating in the study or may influence the results of the study or the subject's ability to participate in the study
4. Any clinically relevant lung disease, other than COPD considered by the investigator to be the primary diagnosis. For example mild-to-moderate bronchiectasis is acceptable in addition to COPD unless the bronchiectasis is considered to be the primary diagnosis
5. An alternative cause for the increase in symptoms of COPD that are unrelated to an exacerbation such as:
5.1. Suspicion or clinical evidence of pneumonia
5.2. High probability and suspicion of pulmonary embolism
5.3. Suspicion or clinical evidence of a pneumothorax
5.4. Primary ischaemic event – ST or Non ST elevation myocardial infarct and left ventricular failure [i.e. not an exacerbation of COPD]
6. A known allergy to the IMP (prednisolone), NIMP (doxycycline) or to any of the constituents of the placebo
7. Patients on maintenance corticosteroids (prednisolone, hydrocortisone, fludrocortisone)
8. Known adrenal insufficiency
9. Currently enrolled in another CTIMP trial and receiving an intervention as part of the trial
10. Pregnant and breastfeeding women

Date of first enrolment
18/09/2017

Date of final enrolment
31/12/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Bicester Health Centre
The Health Centre
Coker Close
Bicester
United Kingdom
OX26 6AT

Study participating centre
Broadshires Health Centre
Broadshire Way
Carterton
United Kingdom
OX18 1JA

Study participating centre
Montgomery House Surgery
Piggy Lane
Bicester
United Kingdom
OX26 6HT

Study participating centre
White Horse Medical Practice
Faringdon Medical Centre
Volunteer Way
Faringdon
United Kingdom
SN7 7YU

Study participating centre
Eynsham Medical Centre
Conduit Ln
Eynsham

Witney
United Kingdom
OX29 4QB

Study participating centre
Windrush Medical Practice
Welch Way
Oxfordshire
Whitney
United Kingdom
OX28 6JS

Study participating centre
Gladstone Surgery
Chess Medical Centre
260-290 Berkhampstead Rd
Chesham
United Kingdom
HP5 3EZ

Study participating centre
Alchester Medical Group
9 Nightingale Pl
Bicester
United Kingdom
OX26 6XX

Study participating centre
Woodlands Medical Centre
Woodlands Rd
Didcot
United Kingdom
OX11 0BB

Study participating centre
Haddenham Medical Centre
Stanbridge Rd
Haddenham
Aylesbury
United Kingdom
HP17 8JX

Study participating centre
Morland House Surgery
London Rd
Wheatley
Oxford
United Kingdom
OX33 1YJ

Study participating centre
Norden House Surgery
Avenue Rd
Winslow
Buckingham
United Kingdom
MK18 3DW

Study participating centre
The Swan Practice
North End
High Street
Buckingham
United Kingdom
MK18 1NU

Study participating centre
Whitchurch Surgery
49 Oving Rd
Whitchurch
Aylesbury
United Kingdom
HP22 4JF

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR Trainees Co-ordinating Centre (TCC); Grant Codes: PDF-2013-06-052

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.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet version V6.0	11/11/2025	11/11/2025	No	Yes
Protocol file		08/04/2019	02/12/2020	No	No