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Biomarkers to target antibiotics and steroid therapy in chronic obstructive pulmonary disease (COPD) exacerbations

Submission date 28/05/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/07/2009	**Overall study status** Completed	
Last Edited 12/09/2012	**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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
G0601369

Study information

Scientific Title
The use of biomarkers to direct antibiotic and systemic corticosteroid therapy in chronic obstructive pulmonary disease (COPD) exacerbations: a randomised controlled study

Acronym
BEAT:COPD

Study objectives
Chronic obstructive pulmonary disease (COPD) is a common condition associated with significant morbidity and mortality. It is predicted to be the third leading cause of death worldwide by 2020. COPD exacerbations are an important feature of the disease, accounting for significant morbidity, mortality and health care costs.

COPD exacerbations are associated with bacterial and viral respiratory infections and airway inflammation. Current guidelines advocate the use of oral corticosteroids for patients with a COPD exacerbation who have increased dyspnoea and antibiotics in those with a history of more purulent sputum. A Cochrane review for the use of systemic corticosteroids and antibiotics in COPD exacerbations have shown that corticosteroids increase the rate of recovery following a severe exacerbation, reduce the length of hospital admission and reduce the proportion of patients that have treatment failure. However, it is likely these small corticosteroid-related benefits are confined to a sub-group of patients. Likewise antibiotic therapy in COPD exacerbations is beneficial, with a reduction in short-term mortality and treatment failure; however, the range of response was large and it is estimated that antibiotics are of clinical benefit in only 25 - 50% of COPD exacerbations.

Our inability to identify accurately which patients with a COPD exacerbation should receive antibiotics and or corticosteroids inevitably leading to inappropriate and excessive use of treatment, is the basis of our hypothesis and the use of a single or composite to deliver targeted antibiotic and or corticosteroid therapy at the time of a COPD exacerbation.

As of 20/10/2009 this record was updated after a change to the protocol following MHRA approval. All changes can be found under the relevant section with the above update date. Please note that at this time, the following changes were made:
1. The study design has been updated; the initial study design was: 'Randomised controlled study'
2. The target number of participants has changed; the initial target number of participants was: '136'
3. A placebo arm was added to the interventions section; details of this can be found in the interventions section.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Leicestershire, Northamptonshire and Rutland Research Ethics Committee approved in September 2007 (ref: 07/H0406/157)

Study design
Amended 20/10/2009: A randomised biomarker-driven prednisolone/placebo intervention study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

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

Interventions
Current interventions as of 20/10/2009:
Randomised 12-month parallel group study with two study groups:
1. Standard care therapy group: subjects will receive treatment as decided by a physician and complying with the Global Initiative for Chronic Obstructive Lung Disease (GOLD)/National Institute for Health and Clinical Excellence (NICE) guidelines for management of COPD exacerbations. This may include increasing bronchodilators, a short duration of oral corticosteroids plus or minus antibiotic therapy (according to local hospital microbiological guidelines).
2. Biomarker directed therapy group: subjects will be assigned to 14 days of oral prednisolone or matching placebo as guided by the biomarker and/or 7 days (maximum) of antibiotic therapy.

Randomisation by minimisation: COPD severity, eosinophilic airway inflammation, exacerbation frequency from previous 12 months. Each arm of the study will be followed up for 12 months.

Initial interventions at time of registration:
Randomised 12-month parallel group study with two study groups:
1. Standard care therapy group: subjects will receive treatment as decided by a physician and complying with the Global Initiative for Chronic Obstructive Lung Disease (GOLD)/National Institute for Health and Clinical Excellence (NICE) guidelines for management of COPD exacerbations. This may include increasing bronchodilators, a short duration of oral corticosteroids plus or minus antibiotic therapy (according to local hospital microbiological guidelines).
2. Biomarker directed therapy group: subjects will be assigned to 14 days of oral prednisolone and/or 7 days (maximum) of antibiotic therapy or neither as guided by the biomarker.

Randomisation by minimisation: COPD severity, eosinophilic airway inflammation, exacerbation frequency from previous 12 months. Each arm of the study will be followed up for 12 months.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Proportion of exacerbations treated with antibiotics and corticosteroids
2. Proportion of exacerbations that are associated with a treatment failure
3. Change in health status

Looked at within 3 months of the completion of the study.

Added 20/10/2009:
The study has 80% powering to show equivalence in a minimal change of health status (0.5: measured by the mCRQ).

Secondary outcome measures
1. Change in forced expiratory volume in one second (FEV1)
2. Markers of airway inflammation
3. Number of adverse reactions

Looked at within 3 months of the completion of the study.

Overall study start date
01/09/2009

Completion date
01/09/2010

Eligibility

Key inclusion criteria
1. Provision of informed consent
2. Male or female
3. Aged 40 years or over
4. Diagnosis of COPD
5. Greater than one exacerbation requiring antibiotics and or corticosteroids in the preceding year

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
106 (standard therapy arm: 53; biomarker arm: 53)

Key exclusion criteria

1. Current active respiratory tuberculosis
2. Upon questioning the patient known human immunodeficiency virus (HIV) infection or positive hepatitis B or C
3. Known inability to produce a sputum sample during the induced sputum procedure
4. 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
5. Any clinically relevant lung disease other than COPD
6. Donation of blood within 3 months or during the study (for other than study purpose)
7. Pregnancy or lactation

Date of first enrolment
01/09/2009

Date of final enrolment
01/09/2010

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Glenfield Hospital
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LE3 9QP

Sponsor information

Organisation
University Hospitals of Leicester NHS Trust (UK)

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Sponsor type
Hospital/treatment centre

Website
http://www.uhl-tr.nhs.uk/

ROR
https://ror.org/02fha3693

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK) (ref: G0601369)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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	01/07/2012		Yes	No