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3TR-ABC multi-scale multiomic analysis of mild /moderate asthma and healthy controls

Submission date
02/02/2024

Recruitment status
Recruiting

Registration date
06/02/2024

Overall study status
Ongoing

Last Edited
07/05/2025

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
Asthma affects over 350 million people in the world. Approximately 5-10% of people with asthma have severe disease. Asthma is a lung disease associated with inflammation (swelling) of the airways. Certain proteins made by the body, called interleukins, can make this inflammation worse. White blood cells (called eosinophils) are also involved in the inflammation of the airways. In recent years, new treatment options have been developed. These new treatments, called biological drugs, have been shown to improve quality of life and reduce the use of high doses of steroids which are heavy in side effects. The challenge with biological drugs is that not all patients benefit or fully benefit from the treatment. Thus, there is a need for a better understanding of which patients will and will not benefit from biological drugs.

As part of this sub-study, people with mild/moderate asthma and healthy people with or without an underlying lung disease will be included as reference groups or ‘controls’ and will undergo the same baseline visit as patients with severe asthma. It is important to have ‘controls’ so that researchers can compare different factors with the investigation population of the study (i.e. in this study, patients with severe asthma). By doing this sub-study we hope to be able to obtain information that may help to improve asthma treatment in the future.

Who can participate?
Adults aged 18 years and over with mild/moderate asthma, and healthy people with or without an underlying lung disease.

What does the study involve?
Participants with mild/moderate asthma and healthy people with or without an underlying lung disease will be included as reference groups or ‘controls’ and will undergo the same baseline visit as patients with severe asthma. It is important to have ‘controls’ so that researchers can compare different factors with the investigation population of the study (i.e. in this study, patients with severe asthma).

What are the possible benefits and risks of participating?
There is no guarantee that participants will receive any benefit from this study, and taking part in this study may or may not improve their asthma (where applicable). Information from this study may help asthma treatment in the future.

There are possible risks, disadvantages and inconveniences with any research study. The individual risks to each procedure and investigation are described fully earlier on in the information sheet. Consider these carefully before agreeing to take part in this study. As part of the sub-study, participants will be asked to attend their local research site to complete the baseline visit. The study visit can last approximately 3 to 4.5 hours, however it may be performed over several days if they wish. Participants will also have more tests and procedures than they normally would if they take part in the study.

Where is the study run from?
This is a research project organised by the NIHR Leicester Biomedical Research Centre – Respiratory at Glenfield Hospital. This study is part of a larger programme of studies, called 3TR. 3TR is a European research group aimed at improving the treatment of asthma and COPD. This study is being conducted by a group of clinical and academic experts from UK universities and Europe, together with pharmaceutical companies who have an interest in asthma. The sponsor of the study is the University of Leicester (UK). The sponsor is the organisation responsible for ensuring that the study is carried out correctly.

When is the study starting and how long is it expected to run for?
March 2023 to December 2026

Who is funding the study?
Innovative Medicines Initiative (Belgium)

Who is the main contact?
1. UK project management team, abc-3tr@leicester.ac.uk
2. Prof Chris Brightling, ceb17@leicester.ac.uk

Study website
https://3trbio.com/

Contact information

Type(s)
Public

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Type(s)
Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
323812

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
0902, IRAS 323812, CPMS 55639

Study information

Scientific Title
3TR-ABC multiomics in asthma and healthy controls

Acronym
3TR-ABC multiomics

Study objectives
Asthma remission following treatment with biologics is related to baseline phenotype and biomarker(s) or early changes in biomarkers.

Patients with mild/moderate controlled asthma and healthy controls will act as a reference population for baseline biomarkers of asthma remission.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 18/12/2023, Nottingham 1 Research Ethics Committee (Health Research Authority, 2nd Floor, Equinox House, City link, Nottingham, NG2 4LA, United Kingdom; +44 (0)2071048115; Nottingham1.rec@hra.nhs.uk), ref: 23/EM/0072

Study design
Multi-centre multi-national observational study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital, Internet/virtual, Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Mild/moderate asthma and healthy volunteers

Interventions
Patients with mild/moderate controlled asthma and healthy individuals will be included as reference (control) groups and will undergo the same baseline visit as patients with severe asthma. Data from the study will be used as a comparison for the TezeBIO study (https://www.isrctn.com/ISRCTN75982397), DupiBIO study (https://www.isrctn.com/ISRCTN68147929), and MepoBIO study (https://www.isrctn.com/ISRCTN47298476). Up to 50 healthy controls (age, sex, and smoking history matched) and 50 mild/moderate asthma controls (minimum matched according to age, sex, and smoking history) will be recruited.

This study is aligned with the 3TR (taxonomy, treatment, targets and remission) EU-IMI consortium asthma biologics cohort (3TR-ABC).

Intervention Type
Other

Primary outcome measure
1. Adequacy of asthma control and change in asthma control measured using the Asthma Control Questionnaire 5 Questions (ACQ5) <1.5, assessed at 1 year

2. Pulmonary function measured using post-bronchodilator (post-BD) Forced Expiratory Volume in 1 Second (FEV1) percent predicted, at 1 year
3. Exacerbations history, assessed using medical history at 1 year
4. Oral corticosteroids use, assessed using medical history and current medications at 1 year

Secondary outcome measures

1. Patient-reported outcomes (* indicates only in mild/moderate asthma controls):
1.1. Adequacy of asthma control and change in asthma control measured using the Asthma Control Questionnaire 5 Questions (ACQ5), assessed at visit 1 (week 0).*
1.2. Physical and emotional impact of asthma measured using Asthma Quality of Life Questionnaire (AQLQ), assessed at visit 1 (week 0).*
1.3. Health-related quality of life measured using the EQ5D5L health status questionnaire, assessed at visit 1 (week 0).
1.4. Effect of health problems on the ability to work and perform regular activities measured using the Work Productivity and Activity Impairment General Health (WPAI:GH) questionnaire, assessed visit 1 (week 0).*
1.5. Quality of life and symptom control in allergic rhinitis measured using the Sino-Nasal Outcome Test-22 Questionnaire (SNOT22), assessed visit 1 (week 0).*
1.6. Symptoms associated with dysfunctional breathing patterns measured using the Nijmegen Questionnaire (NQ), assessed during visit 1 (week 0).*
1.7. Subjective measure of sleepiness measured using the Epworth Sleepiness Scale (ESS), assessed visit 1 (week 0).
1.8. Symptoms of anxiety and depression measured using the Hospital Anxiety and Depression Scale (HADS), assessed visit 1 (week 0).
1.9. Level of fatigue during daily activities measured using the Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scale, assessed at visit 1 (week 0).*
1.10. Cognition measured using the Cognitive Failures Questionnaire, Screen for Cognitive Impairment in Psychiatry (SCIP), Trail Making test (TMT) part B (specific sites), assessed at visit 1 (week 0).
1.11. Treatment effectiveness measured using the Visual analogue scale (VAS) scale 3TR question (patient and physician perceived), assessed at visit 1 (week 0).*
1.12 Symptoms measured using Symptoms VAS at visit 1 (week 0).*

2. Lung function measured using:
2.1. Pre and post-BD spirometry, assessed at visit 1 (week 0).
2.2. Fractional Exhaled Nitric Oxide (FeNO) at visit 1 (week 0).

3. Biomarkers measured using:
3.1. Blood: differential cell count, total IgE and transcriptome (and in a subgroup scRNA), assessed at visit 1 (week 0). Specific IgE if not done with skin prick tests (cat dander, dog dander, house dust mite, grass pollen and Aspergillus IgE) and immunophenotyping, methylome (DNA collected for possible later eQTL analyses depending upon transcriptome data), assessed at visit 1 (week 0).
3.2. Nasal sampling: nasal brushings, assessed at visit 1 (week 0).
3.3. Breath: Fractional exhaled nitric oxide (FeNO), and ReCIVA for breathomics, assessed at visit 1 (week 0).
3.4. Sputum: cell differential, transcriptome, micro/metagenomics and proteomics, assessed at visit 1 (week 0).
3.5. Saliva: Microbiome analysis and DNA, assessed at visit 1 (week 0).
3.6. Urine: Urinary lipid mediators and metabolomics, assessed at visit 1 (week 0).
3.7. Thoracic CT (specific sites), assessed at visit 1 (week 0).
3.8. Stool (optional): micro/metagenomics, assessed at visit 1 (week 0).

3.9. Bronchoscopy (optional): brush biopsy, bronchial biopsies and broncho-alveolar lavage (BAL) for transcriptome, protein, micro/metagenomics, cellular and structural analyses, assessed at visit 1 (week 0).
3.10. Mucosal biopsies: histological analysis of cells and inflammatory mediators, assessed at visit 1 (week 0).

Overall study start date
01/03/2023

Completion date
31/12/2026

Eligibility

Key inclusion criteria
Mild/moderate asthma controls
1. Adult (≥18 years old)
2. Diagnosed with mild/moderate controlled asthma:
2.1 Low/medium dose of ICS/LABA +/- LTRA
2.2 ACQ < 1.5
2.3 Markers of T2 inflammation (B-eos ≥ 0.15 actual or ≥ 0.30 the last year or Sputum eos ≥ 3%, FeNO ≥ 25, allergens positivity)
2.4 Markers of T2 low inflammation (B-eos < 0.15 actual or < 0.30 the last year of sputum eos < 3%, FeNO < 25, allergens negativity)
2.5 No exacerbations in the past 12 months
2.6 No need for prednisolone treatment
2.7 Not a direct candidate for biologic therapy
3. Be able to give valid written consent, and compliant with study procedures and study visits.

Healthy controls
1. Adult (≥18 years old)
2. Healthy:
2.1 No current medication/therapy for autoimmune, inflammatory, or allergic diseases
2.2 No history of asthma or respiratory symptoms
2.3 No history of allergies
2.4 No upper or lower respiratory infections in the past 4 weeks
3. Be able to give valid written consent, compliant with study procedures and study visits

Participant type(s)
Healthy volunteer, Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

Up to 50 healthy controls and 50 mild/moderate asthma controls

Key exclusion criteria
Mild/moderate asthma controls
1. Unable to understand written information due to language barriers.
2. Unable to give informed consent, i.e., patients who are incapable.
3. Unable to complete study visits.

Healthy controls
1. Unable to understand written information due to language barriers.
2. Unable to give informed consent, i.e., patients who are incapable.
3. Unable to complete study visits.

Date of first enrolment
31/08/2023

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
University Hospitals of Leicester NHS Trust
Glenfield Hospital
Groby Rd
Leicester
United Kingdom
LE3 9QP

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road Glasgow
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G12 0XH

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

Sponsor information

Organisation
University of Leicester

Sponsor details
Research & Enterprise Division
Research Ethics
Governance & Integrity Office
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Sponsor type
University/education

Website
https://le.ac.uk/research/regi

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Research council

Funder Name
Innovative Medicines Initiative

Alternative Name(s)

The Innovative Medicines Initiative, Europe's Innovative Medicines Initiative, EU Innovative Medicines Initiative, IMI

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Belgium

Results and Publications

Publication and dissemination plan
A publication plan will be written by the Trial Management Group (TMG) and the Patient and Public Involvement (PPI) group during the study with the sponsor and funder approvals. It is envisaged that the results of the study will be published in newsletters and presented in public webinars for participants, lay media and the relevant peer-reviewed journals. Results will be provided by the local clinical teams to the participants at the end of the study.

Intention to publish date
31/08/2028

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication