

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

<b>Submission date</b>	<b>Recruitment status</b>	<input type="checkbox"/> Prospectively registered
02/02/2024	No longer recruiting	<input type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
06/02/2024	Ongoing	<input type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
07/05/2025	Respiratory	<input checked="" type="checkbox"/> 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

# Contact information

## Type(s)

Public

## Contact name

Miss Bonnie Millar

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**Type(s)**

Scientific, Principal investigator

**Contact name**

Prof Christopher Brightling

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## Additional identifiers

**Clinical Trials Information System (CTIS)**

Nil known

**Integrated Research Application System (IRAS)**

323812

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

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

## **Study type(s)**

Treatment

## **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(s)**

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

## **Key secondary outcome(s)**

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).

## Completion date

31/12/2026

## Eligibility

### Key inclusion criteria

**Mild/moderate asthma controls**

1. Adult ( $\geq 18$  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  $\geq 0.15$  actual or  $\geq 0.30$  the last year or Sputum eos  $\geq 3\%$ , FeNO  $\geq 25$ , 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 ( $\geq 18$  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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**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**

United Kingdom

England

Scotland

**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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**Study participating centre**

**University Hospital Southampton NHS Foundation Trust**

Southampton General Hospital

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## Sponsor information

**Organisation**

University of Leicester

**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

### 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

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes