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Biomarkers of asthma remission after mepolizumab treatment

Submission date 10/05/2023	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 12/05/2023	**Overall study status** Ongoing	
Last Edited 12/05/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims

Asthma affects over 350 million people in the world. About 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. One of these interleukin proteins is called interleukin-5 (IL5). Interleukin-5 appears to play an important role in asthma. It plays a role by helping white blood cells (called eosinophils) stay alive. Eosinophils are involved in the inflammation of the airways.

Mepolizumab is a medicine that blocks the effect of Interleukin-5 on eosinophils (and therefore reduces inflammation). It is given as an injection under the skin and may help reduce inflammation in the airways of people with asthma. Previous research studies in people with severe asthma have shown an improvement in asthma control in those who received mepolizumab, and it is now approved for the treatment of severe asthma in the UK.

Research studies have shown that people who received mepolizumab experienced about half as many asthma exacerbations (severe episodes of asthma or attacks) compared to those given placebo (dummy) injections. In addition, it also improved their lung function and asthma control.

In this research study the researchers want to observe all participants having mepolizumab injections as part of their normal clinical care. They would like to try and understand what might be causing the high levels of disease control, including the absence of symptoms and exacerbations. By doing this they hope to be able to obtain information that may help to improve asthma treatment in the future.

The researchers will study the effect of the medicine ‘mepolizumab’ on all aspects of asthma such as changes in quality of life, symptoms, inflammation and breathing tests.

Who can participate?

Patients aged 18 years and over following a clinical decision to start mepolizumab treatment for severe asthma after meeting licensing, local and national guidelines.

What does the study involve?

Every participant will be receiving mepolizumab injections as part of their normal clinical care. In between study visits participants will be asked to complete some breathing tests at home. They will be asked to monitor their peak flow (maximum rate a person can breathe out) and a test for exhaled nitric oxide (FeNO) every day for the first 4 weeks of the study and then once a week

afterwards. This is to monitor the usual variation in their asthma symptoms and airway function, and how this might change if they become unwell.

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. 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 of each procedure and investigation are described fully in the participant information sheet. Participants will also potentially have more tests and procedures if they take part in the study, compared to standard hospital visits. Study visits could take more time than standard hospital visits and they will have more blood taken. Each study visit can last 1-3 hours. They will have to do additional monitoring of their asthma at home as the study requires them to keep track of their peak flow reading and lung inflammation with FeNO (about 10 minutes).

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 2028

Who is funding the study?
GlaxoSmithKline

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

Contact information

Type(s)
Principal investigator

Contact name
Prof Christopher Brightling

ORCID ID
https://orcid.org/0000-0002-9345-4903

Contact details
Department of Respiratory Sciences
University of Leicester
NIHR Leicester Biomedical Research Centre – Respiratory
Glenfield Hospital
Groby Road

Leicester
United Kingdom
LE3 9PQ
+44 (0)116 250 2704
abc-3tr@leicester.ac.uk

Type(s)
Public

Contact name
Miss Bonnie Millar

Contact details
Department of Respiratory Sciences
University of Leicester
Glenfield Hospital
Groby Road
Leicester
United Kingdom
LE3 9QP
+44 (0)116 252 2893
abc-3tr@leicester.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
323811

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
UoL0893, IRAS 323811, CPMS 55640

Study information

Scientific Title
Biomarkers and mechanisms of asthma remission following treatment with mepolizumab in adults with severe asthma – 3TR ABC

Acronym
MEPOBIO – 3TR ABC

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

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 20/04/2023, East Midlands - 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/0071

Study design
Multi-centre multi-national observational study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Severe asthma

Interventions
Current interventions as of 30/07/2024:

MEPOBIO – 3TR ABC is a multi-centre observational study of patients with severe asthma following initiation of treatment with mepolizumab (anti-IL5) as part of their standard of care. Participants will be extensively characterised at baseline; reviewed throughout the year with formal clinical and biological assessment at 4, 16, 52 weeks, 2 years and 3 years. Asthma remission will be defined for each domain: asthma control, lung function, and exacerbations as a composite measure and independently. Biomarkers and multi-omic analysis will be undertaken in the biosamples to determine biological pathways and bio-signatures associated with asthma remission. Primary outcome will be assessed at 1 year. This study is one of three arms aligned to the 3TR (taxonomy, treatment, targets and remission) EU-IMI consortium asthma biologics consortium (3TR-ABC).

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Previous interventions:

MEPOBIO – 3TR ABC is a multi-centre observational study of patients with severe asthma following initiation of treatment with mepolizumab (anti-IL5) as part of their standard of care. Participants will be extensively characterised at baseline; reviewed throughout the year with formal clinical and biological assessment at 4, 16, 24, 52 weeks, 2 years and 3 years. Asthma remission will be defined for each domain: asthma control, lung function, and exacerbations as a composite measure and independently. Biomarkers and multi-omic analysis will be undertaken in the biosamples to determine biological pathways and bio-signatures associated with asthma remission. Primary outcome will be assessed at 1 year. This study is one of three arms aligned to the 3TR (taxonomy, treatment, targets and remission) EU-IMI consortium asthma biologics consortium (3TR-ABC).

Intervention Type
Drug

Phase
Not Applicable

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

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))
Current secondary outcome measures as of 30/07/2024:

1. Patient-reported outcomes:
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), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.2. Physical and emotional impact of asthma measured using Asthma Quality of Life Questionnaire (AQLQ), assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.3. Quality of life in people with severe asthma measured using the Self-Assessment Questionnaire (SAQ), assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.4. Health-related quality of life measured using the EQ5D5L health status questionnaire, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.5. Effect of health problems on 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), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.6. Quality of life and symptom control in allergic rhinitis measured using the Sino-Nasal Outcome Test-22 Questionnaire (SNOT22), assessed visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.7. Symptoms associated with dysfunctional breathing patterns measured using the Nijmegen Questionnaire (NQ), assessed visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.8. Subjective measure of sleepiness measured using the Epworth Sleepiness Scale (ESS), assessed visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.9. Symptoms of anxiety and depression measured using the Hospital Anxiety and Depression Scale (HADS), assessed visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.10. Level of fatigue during daily activities measured using the Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scale, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.11. Cognition measured using the Cognitive Failures Questionnaire, Screen for Cognitive Impairment in Psychiatry (SCIP), Trail Making test (TMT) (specific sites), assessed at visit 1 (week

0), visit 3 (week 16) and visit 4 (week 52).
1.12. Treatment effectiveness measured using the Global evaluation treatment efficacy (GETE), patient and physician-related response, assessed at visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.13. Treatment effectiveness measured using the Visual analogue scale (VAS) scale 3TR question (patient and physician perceived), assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).

1.14 Symptoms measured using the Symptoms VAS at (patient and physician perceived), assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.

2. Lung function measured using:
2.1. Pre and post BD spirometry, assessed at visit 1 (week 0).
2.2. Post BD Forced Expiratory Volume in 1 Second (FEV1) assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.

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), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years). 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), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
3.3. Breath: Fractional exhaled nitric oxide (FeNO) assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit; and breathomics assessed at visit 1 (week 0), visit 2 (week 4), visit 4 (week 52).
3.4. Sputum: cell differential, transcriptome, micro/metagenomics and proteomics, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
3.5. Saliva: Microbiome analysis and DNA, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
3.6. Urine: Urinary lipid mediators and metabolomics, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
3.7. Stool (optional): micro/metagenomics, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
3.8. 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).
3.9. Mucosal biopsies: histological analysis of cells and inflammatory mediators, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).

Previous secondary outcome measures as of 19/01/2024:

1. Patient-reported outcomes:
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), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.2. Physical and emotional impact of asthma measured using Asthma Quality of Life Questionnaire (AQLQ), assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
1.3. Quality of life in people with severe asthma measured using the Self-Assessment Questionnaire (SAQ), assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
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1.5. Effect of health problems on 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), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
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3.2. Nasal sampling: nasal brushings, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
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Previous secondary outcome measures:

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3.3. Breath: Fractional exhaled nitric oxide (FeNO) and breathomics, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
3.4. Sputum: cell differential, transcriptome, micro/metagenomics and proteomics, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
3.5. Oral gargle: Microbiome analysis, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
3.6. Urine: Urinary lipid mediators and metabolomics, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years), and unscheduled exacerbation visit at sites where feasible/applicable.
3.7. Stool (optional): micro/metagenomics, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).
3.8. 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).
3.9. Mucosal biopsies: histological analysis of cells and inflammatory mediators, assessed at visit 1 (week 0), visit 2 (week 4), visit 3 (week 16), visit 4 (week 52), visit 5 (2 years), visit 6 (3 years).

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Adults (≥18 years old)
2. Clinical decision to initiate mepolizumab for severe asthma after meeting licensing, local and national guidelines
3. Be able to give valid written consent. Participants should have a reasonable understanding of the English language (assessed by the research team)
4. Compliant with study procedures and study visits

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Known hypersensitivity to the active substance of mepolizumab or any of the excipients
2. Participation in an interventional clinical trial within 3 months of visit 1 or receipt of any investigational medicinal product within 3 months or 5 half-lives. Participation in other observational studies is acceptable if in the view of the investigator it will not impact the study outcomes
3. Other clinically significant medical disease or uncontrolled concomitant disease that is likely, in the opinion of the investigator, to require a change in therapy or impact the ability to participate in the study

Date of first enrolment
31/08/2023

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

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

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

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

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

Study participating centre
Belfast Health and Social Care Trust
Trust Headquarters
A Floor - Belfast City Hospital
Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre
Guys and St Thomas' NHS Foundation Trust
Sydney Street
London
United Kingdom
SW3 6NP

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location

United Kingdom

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?
HRA research summary			20/09/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes