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Responses to mepolizumab in real world treatment of severe asthma

Submission date 13/11/2026	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 16/11/2026	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 16/11/2026	**Condition category** Respiratory	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Mepolizumab has been introduced as biologic treatment for severe asthma targeting the cytokine IL-5 that drives part of the eosinophilic inflammation being a key feature in asthmatic inflammation. Although clinical trials during the drug development process have established that many patients with severe asthma respond well to this new treatment, it remains to determine which patients in a real-life clinical setting respond favourably to mepolizumab and which factors that determine the responsiveness. This study is focused on improved methods to assess the clinical response and new predictive biomarkers to aid precision medicine decisions.

Who can participate?
Males and females aged 18 years or older with severe asthma diagnosed in the specialist care setting. Everyone must give written informed consent before taking part.

What does the study involve?
Patients who have been selected for treatment with mepolizumab by the clinical severe asthma team are after the decision has been made invited to participate in the research project. After consent has been obtained, a thorough medical history, extensive clinical examinations and collection of samples for biochemical and immunological measurements of markers in blood, urine, saliva and exhaled air are performed at baseline before the start of the treatment with mepolizumab. The majority of examinations and samplings are repeated after 4 months, 1 year, 2 years and 3 years on the treatment. At all visits, the patients also report symptoms and quality of life measures by the use of standardised questionnaires.

What are the possible benefits and risks of participating?
There is no direct benefit to participate in the research project above the potential benefit of improved asthma due to the effects of the treatment decided on clinical grounds. However, the information collected may help improve future diagnosis and treatment of asthma for similar patients. In addition, it is our experience from previous projects that patients who participate in this type of research with long study visits and prolonged follow-up visits learn much about their condition and thereby improve self management.
The risks are small and would relate to giving different biological samples (blood, urine, saliva and exhaled breath), such as e.g. brief discomfort or bruising during sampling of blood.

Where is the study run from?
The study is carried out at the Departments of Lung and Allergy Diseases at the Karolinska Hospital in Stockholm and the Academic Hospital in Uppsala, both centres in Sweden.

When is the study starting and how long is it expected to run for?
June 2017 to September 2025.

Who is funding the study?
Academic funds and investigator-initiated industry support (GSK).

Who is the main contact?
Prof. Sven-Erik Dahlén, sven-erik.dahlen@ki.se

Contact information

Type(s)
Principal investigator, Scientific, Public

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Additional identifiers

Study information

Scientific Title
The BIOCROSS cohort for real-world assessment of biomarkers and clinical responses to mepolizumab in severe eosinophilic asthma

Acronym
BIOCROSS-MEPO

Study objectives
1. To test a new composite scoring system (COMSA) for grading of the clinical response to the treatment

2. To determine which baseline biomarkers before treatment that predict short-term as well as long term clinical outcomes
3. To determine response biomarkers that provide quantitative objective measures of target engagement, treatment effectiveness, and mechanisms of action

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 16/06/2017, Regional Ethics committee in Stockholm, Sweden, decision registration no 2017/832-31/1 (Karolinska Institutet, Stockholm, SE-17177, Sweden; +46 852486000; epm@etikprovning.se), ref: 2017/832-31/1

Primary study design
Observational

Secondary study design
Cohort study

Study type(s)

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

Interventions
Patients who have been selected for treatment with the anti-IL5 biologic mepolizumab by the clinical severe asthma team are after the decision has been made invited to participate in the research project. After consent has been obtained, a thorough medical history, extensive clinical examinations and collection of samples for biochemical and immunological measurements of markers in blood, urine, saliva and exhaled air are performed at baseline before the start of the treatment with mepolizumab. The majority of examinations and samplings are repeated after 4 months, 1 year, 2 years and 3 years on the treatment. At all visits, the patients also report symptoms and quality of life measures by the use of standardised questionnaires.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Mepolizumab (Nucala ®) 100 mg subcutaneously every fourth week during three years of follow-up

Primary outcome(s)
1. Conventional clinical outcomes measured using changes in conventional clinical outcomes such as asthma symptoms, lung function, use of asthma medications including oral corticosteroids (OCS), number of asthma exacerbations at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

2. Clinical effect of the treatment measured using COMSA (Core Outcome Measures sets Severe Asthma. COMSA is a new composite score with five domains (OCS use, exacerbations, lung function, asthma control score [ACT-5], and asthma specific quality of life score [AQLQ], see Khaleva et al ERJ 2022:2200606) at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

3. Predictive biomarkers measured using relation between clinical effect as determined by 1 and 2 above and baseline markers of type 2 (T2) inflammation (Blood eosinophil level, Exhaled nitric oxide (FeNO), urinary lipid mediators, periostin etc) at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

4. Response biomarkers measured using influence of the intervention on biomarker profiles, i.e. molecular response monitoring at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

Key secondary outcome(s)

1. Lymphocyte dynamics measured using influence of the intervention on circulating lymphocytes, and in particular the T2 associated ILC2 cells, determined by FACs analysis in PBMCs at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

2. Mast cell markers measured using influence of the intervention on mast cell markers in blood and urine at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

3. Steroid hormones measured using influence of the intervention on steroid hormones, in particular endogenous androgens, as assessed by mass spectrometry measurement of metabolites in urine. at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

4. Lipid mediator profiles (Eicosanoids) measured using influence of the intervention on global profile of metabolites of bioactive lipid mediators as assessed by mass spectrometry measurements in urine at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

5. Small airways function measured using influence of the intervention on small airways as assessed by IOS (Impulse OScillometry) at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

6. Proteomics measured using influence of the intervention on protein profile as measured in plasma by Olink 5400 Explorer methodology at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

7. Transcriptomics measured using influence of the intervention on blood transcriptomic profile at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

8. Metabolomics measured using influence of the intervention on sphingolipid profile and other small molecules in blood measured by mass spectrometry at baseline before treatment and follow-ups at 4 months, 1 year, 2 years, and 3 years

Completion date

15/09/2025

Eligibility

Key inclusion criteria
1. Men and women above age of 18 years
2. General: Able to give written informed consent and able to read, comprehend, and write at a sufficient level to complete study related materials
3. Severe asthma: Meeting internationally recognised criteria for diagnosis of severe asthma including to have been under the follow up of a respiratory specialist for at least 6 months prior to enrolment in the study. During this time appropriate investigations should have been performed to exclude other diagnoses and steps taken to optimise asthma control including treatment of co-morbidities, assessment of adherence, and reduction in allergen exposure in sensitised subjects

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
78

Key exclusion criteria
1. Subject has changed asthma medication within the 4 weeks prior to screening (except those using the Symbicort maintenance and reliever therapy)
2. Subject had a severe asthma exacerbation (requiring high dose OCS or a doubling of maintenance OCS for at least 3 days) in the previous month
3. Significant alternative diagnoses that may mimic or complicate asthma, in particular dysfunctional breathing, panic attacks, and overt psychosocial problems (if these are thought to be the major problem rather than in addition to severe asthma)
4. Significant other primary pulmonary disorders in particular pulmonary embolism, pulmonary hypertension, interstitial lung disease and lung cancer
5. Subjects with emphysema and bronchiectasis should only be excluded if this is thought to be the major pulmonary disorder rather than in addition to severe asthma
6. Diagnosis or current investigation of occupational asthma
7. Diagnosis of chronic inflammatory diseases other than asthma (inflammatory bowel disease, rheumatoid arthritis)
8. Alcohol or narcotic abuse

Date of first enrolment
27/06/2017

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
Sweden

Study participating centre
Departments of Lung and Allergy Diseases at the Karolinska Hospital in Stockholm and the Academic Hospital in Uppsala
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Sponsor information

Organisation
Karolinska University Hospital Stockholm, part of Region Stockholm County Council

Funder(s)

Funder type

Funder Name
Academic funds and investigator-initiated industry support (GSK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 3.0	05/10/2019	16/11/2026	No	No