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Understanding the role of neutrophil enzymes in a type of asthma with low inflammation

Submission date
11/12/2025

Recruitment status
Not yet recruiting

Registration date
28/04/2026

Overall study status
Ongoing

Last Edited
18/05/2026

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
Asthma is a common long-term condition that affects the airways and makes breathing difficult. While many people with asthma respond well to standard treatments, about one in ten have a form called type 2-low asthma. This type is particularly hard to treat, as current medicines such as inhaled steroids and biologic therapies are often ineffective. People with type 2-low asthma tend to have more hospital visits, more severe attacks, and a poorer quality of life. A possible reason for this form of asthma is the presence of higher numbers of a type of immune cell called neutrophils in the airways. When activated, neutrophils release proteins including neutrophil elastase that can damage the airway lining and worsen inflammation. Recent research in other lung diseases has shown that medicines which block neutrophil activity may help reduce flare-ups. However, these treatments have not yet been studied in people with type 2-low asthma. This project will investigate whether neutrophil proteins, particularly neutrophil elastase, are increased in people with type 2-low asthma compared to those with other types of asthma.

Who can participate?
Patients with moderate-to-severe asthma from NHS Tayside.

What does the study involve?
Participants will be asked to provide sputum (phlegm) samples, undergo lung function tests, and complete questionnaires about their symptoms and quality of life. The aim is to identify a specific “neutrophilic” form of asthma that may benefit from future treatments targeting neutrophil activity. If successful, this study will provide the foundation for a clinical trial of new medicines, with the ultimate goal of improving symptom control, reducing asthma attacks, and enhance quality of life for those with type 2-low asthma.

What are the possible benefits and risks of participating?
Participants are not expected to benefit directly from taking part. However, their participation may help improve understanding of asthma, particularly the type 2-low phenotype, and could contribute to improved treatments and clinical outcomes in the future.

In terms of risk, sputum induction may cause coughing and temporary discomfort. There is also a potential risk to confidentiality. To minimise these risks, sputum samples can be collected using

a nebuliser with hypertonic saline and strong safeguards are in place to ensure that all participant data are kept secure.

Where is the study run from?
Ninewells Hospital & Medical School, UK.

When is the study starting and how long is it expected to run for?
July 2026 to October 2027.

Who is funding the study?
NHS Tayside, UK.

Who is the main contact?
Dr Rory Chan, r.chan@dundee.ac.uk

Contact information

Type(s)
Principal investigator, Scientific, Public

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Integrated Research Application System (IRAS)
361386

Study information

Scientific Title
Characterising neutrophil serine protease activity in type 2 low asthma

Study objectives
To determine whether sputum neutrophil elastase activity is increased in patients with T2-low asthma compared to T2-high asthma.
To compare other neutrophil-derived proteins (proteinase-3, cathepsin-G, azurocidin-1, neutrophil extracellular trap markers) in patients with T2-low asthma versus T2-high asthma.
To assess relationships between neutrophil protease activity and clinical outcomes such as symptom control, lung function, quality of life, and exacerbation history.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 05/05/2026, West of Scotland REC 4 (1055 Great Western Road, Glasgow, G12 0XH, United Kingdom; -; ggc.wosrec4@nhs.scot), ref: 26/WS/0059

Primary study design
Observational

Secondary study design
Cross sectional study

Study type(s)

Health condition(s) or problem(s) studied
Type 2 inflammatory asthma

Interventions
This is an observational study, which means it will not be testing a new drug or treatment. Instead, the study will carefully study people with asthma to better understand what is happening in their lungs.
The study plans to recruit 120 adults with moderate-to-severe asthma from NHS Tayside. Each patient attending the specialist asthma clinic in Ninewells hospital will be asked whether they would like to participate in this study. At this clinic visit, participants will:
Provide a sputum (phlegm) sample by coughing into a container. This allows us to measure proteins released by
neutrophils, such as neutrophil elastase.
Complete breathing tests (such as spirometry and oscillometry) to measure lung function.
Answer short questionnaires about their asthma symptoms and quality of life.
Provide a small blood sample to measure markers of inflammation.
Afterwards, researchers will analyse the samples in the laboratory. The results will be compared between patients with type 2-low asthma and those with type 2-high asthma. The researchers expect to identify a group of patients with high neutrophil activity who may represent a distinct type of asthma.

Intervention Type
Other

Primary outcome(s)
1. Sputum neutrophil elastase activity, via the concentration of neutrophil elastase in induced sputum in patients with T2-low asthma compared with patients with T2-high asthma measured using a kinetic fluorescence-based neutrophil serine protease activity assay at a single time point

Key secondary outcome(s))
1. Neutrophil-derived proteins (proteinase-3, cathepsin-G, azurocidin-1, and neutrophil extracellular trap markers) concentration levels in induced sputum in patients with T2-low asthma compared with patients with T2-high asthma measured using laboratory assays of neutrophil serine protease activity, azurocidin-1, and neutrophil extracellular trap formation at a single time point

Completion date

01/10/2027

Eligibility

Key inclusion criteria
1. Patients aged ≥18 years old with GINA-defined moderate-to-severe asthma.
2. Taking a medium to high dose of ICS/LABA OR high dose ICS with another second line controller (BDP equivalent dose of ≥800µg) of step 4/5 GINA therapy.
3. Established diagnosis of persistent asthma ≥6 months according to GINA guidelines.
4. Ability to give informed consent.
5. Agreement for their GP to be made aware of study participation and to receive feedback as relevant to the participant's wellbeing.
6. Able to understand the study procedures and the risks involved.
7. Good physical and mental status, determined on the basis of the medical history and a general clinical examination at screening.

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Patients who are taking biologics for asthma.
2. Patients who are on maintenance oral corticosteroids.
3. Patients who have required a course of oral corticosteroids in the past month.
4. Any other respiratory diseases such as COPD and moderate to severe bronchiectasis which in the opinion of the investigator are clinically significant and may have an impact on the study outcomes.
5. Any disorder that is not stable in the opinion of the Investigator.
6. Patients unable or unwilling to consent.
7. Anyone who has had a recent chest infection or asthma exacerbation (within the past 4 weeks), as this may
temporarily alter neutrophil levels in the sputum.
8. People currently taking part in another clinical trial involving investigational medicines or who have received such
medicines within the past 3 months.
9. Individuals with severe comorbidities (such as uncontrolled heart disease, active cancer, or

significant
immunosuppression) where participation may pose additional risk.

Date of first enrolment
18/07/2026

Date of final enrolment
01/10/2027

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Ninewells Hospital
Ninewells Avenue
Dundee
Scotland
DD1 9SY

Sponsor information

Organisation
Asthma + Lung UK

Funder(s)

Funder type

Funder Name
NHS Tayside

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files	version 2	30/01/2026	23/03/2026	No	No
Other files	version 3	28/01/2026	23/03/2026	No	No
Participant information sheet	version 2	22/08/2025	12/12/2025	No	Yes
Participant information sheet	version 5	20/02/2026	23/03/2026	No	Yes
Protocol file	version 6	20/02/2026	23/03/2026	No	No