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Effects of blocking a messaging protein called TSLP (thymic stromal lymphopoietin) on inflammation in the airways

Submission date 12/05/2023	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 14/02/2024	**Overall study status** Ongoing	
Last Edited 12/05/2026	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a highly common chronic lung disease which carries a significant burden for both patients and healthcare systems. Treatment has been limited for several years. Recent studies have shown a promising new target in treating asthma – thymic stromal lymphopoietin (TSLP) is a protein released when the airways are irritated. This causes an increase in airway inflammation and therefore the symptoms of COPD. Blocking or reducing this with a medication called tezepelumab has been shown to reduce airway inflammation in asthma. Other studies have also shown reduced symptoms and exacerbations in a diverse group of asthma patients, including those who do not demonstrate a high level of allergic-type inflammation. This study will investigate the effect of this medication on the airways of people who suffer from COPD.

Who can participate?
People aged over 40 years old with moderate to severe COPD

What does the study involve?
Patients will be recruited to three sites – Copenhagen, Leicester and London. These will be people with moderate to severe COPD, on standard inhaled treatment with at least one exacerbation in the preceding twelve months. Those who are willing to be involved and fulfil screening criteria will have various baseline blood and breathing tests along with questionnaires completed. Everyone will undergo a bronchoscopy – a test where a fine, flexible camera is inserted into the lungs and samples and biopsies can be taken. 50% of people will be randomised to receive the medication and 50% will receive a placebo. Each person and the team looking after them directly will not know which one they are receiving. They will receive this 4 weekly for 5 doses total, then undergo a repeat bronchoscopy and other tests. The total study time will be approximately 22 weeks. If this trial is successful it may contribute to evidence allowing us to use tezepelumab to treat COPD in future.

Participants will be required to undergo two research bronchoscopies. This is generally a safe procedure but rarely serious complications can occur - including bleeding, collapsed lung, cardiac

arrhythmias and very rarely death. This is a key part of the trial as it is the way to obtain the samples which will be studied to look for the effect of the IMP. The risks and benefits will be fully discussed with patients before the procedure in a formal consent process. To minimise risks only patients with FEV1 >30% predicted and >1L will be recruited. All bronchoscopies will be performed in a fully equipped bronchoscopy suite with emergency facilities, by experienced practitioners. A follow-up phone call will be made within 3 days of each bronchoscopy to ensure no adverse events. Some people find bronchoscopy very uncomfortable and can be left with a hoarse voice afterwards. It is also not uncommon to have a temperature in the 24-48 hours after the procedure. Detailed information about the procedure will be available in advance and discussed thoroughly.

What are the possible benefits and risks of participating?
The trial medication may cause some adverse side effects, although in previous studies it has been shown to have a favourable side effect profile. Any adverse events will be managed accordingly.

The study involves 8 visits to the research unit which may cause inconvenience. Participants will receive reimbursement and travel expenses. There are also two phone calls post-bronchoscopy visits. These will be scheduled to occur at a convenient time if possible.

Where is the study run from?
University of Leicester (UK)

When is the study starting and how long is it expected to run for?
May 2023 to July 2027

Who is funding the study?
AstraZeneca (UK)

Who is the main contact?
Mayven Siow, mayven.siow@leicester.ac.uk

Contact information

Type(s)
Principal investigator

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Type(s)
Public, Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05507242

Clinical Trials Information System (CTIS)
2022-000179-38

Integrated Research Application System (IRAS)
1006721

Central Portfolio Management System (CPMS)
60939

Protocol serial number
0886

Study information

Scientific Title
Effects of blocking TSLP on airway inflammation and the epithelial immune response to exacerbation triggers in patients with COPD (UPSTREAM-COPD)

Acronym
UPSTREAM-COPD

Study objectives
To assess the effect of tezepelumab on airway inflammation in people with COPD. We have evidence that this works to reduce airway inflammation in people with severe asthma and wish to investigate if there is a similar effect in COPD, specifically looking at a form of inflammation called eosinophilic inflammation. Eosinophilic inflammation is similar to the changes we see in some forms of asthma.

To investigate the effect of tezepelumab on other forms of airway inflammation, other inflammatory markers, RNA gene expression, markers of airway healing and lung function along with symptom and quality of life questionnaires.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/11/2023, Yorkshire and Humber - Leeds East REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8171, (0)207 104 8357; leedseast.rec@hra.nhs.uk), ref: 23/YH/0117

Primary study design
Interventional

Study design
Randomized placebo-controlled double-blind parallel-group study

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease

Interventions
Participants will be randomised in a 1:1 ratio to IMP versus placebo. The trial team and participants will be blinded to treatment assignment. Randomisation will be stratified based on blood eosinophil counts at baseline (< or≥ 0.2 x109 /L) and smoking status. The blocked randomisation method will be used in this study. Pre-defined clusters of randomised strata will be distributed from the Danish site along with study medication and randomisation in sealed envelopes before the start of the study. Once all eligibility criteria are met, the study nurse will enter the data on smoking status and baseline eosinophil count. The assigned strata with randomised IDs will be subsequently generated.

The drug arm will receive 210 mg tezepelumab, given by subcutaneous injection every 4 weeks for a total of 5 doses. The placebo arm will receive a blinded dose of 0.9% saline subcutaneously at the same frequency and for the same duration. These will be administered by trial staff at each visit. Both arms receive the same follow-up.

The central pharmacy from the Denmark site will be responsible for receiving and labelling IMP for all sites according to a randomisation list prepared by a computerized system. They will inform the local pharmacy/team which numbered vial to administer to each patient as randomised. They will centrally monitor the stock of IMP and placebo in each site, ensuring appropriate stocks are always available. Clinical teams at all sites will be blinded to the intervention.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
The change in eosinophil cell counts in bronchial mucosa is measured using the samples obtained in bronchial biopsy using immunohistochemistry (IHC) at baseline and end of study (week 20)

Key secondary outcome(s)
Evaluating the effect of tezepelumab on bronchial mucosal tissue inflammation by measuring the change in inflammatory cell counts using immunohistochemistry from baseline to week 20

Completion date
31/05/2027

Eligibility

Key inclusion criteria
1. Willing and able to consent to participate in the trial
2. Clinically diagnosed chronic obstructive airway disease with post-bronchodilator FEV1 ≥ 30% to 80% predicted value (and ≥ 1.0 L)
3. Age ≥40 years old
4. Current or ex-smokers with ≥ 10 pack-years of past smoking history
5. Stable airway disease status on maintenance inhaled therapy (LAMA + LABA ± ICS) for at least 3 months prior to screening
6. History of ≥1 moderate-to-severe exacerbation event treated with prednisolone and/or antibiotic in the past 12 months
7. Good compliance with daily inhaler regime (≥70% adherence rate) at screening

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
40 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. History of unstable or severe cardiac, hepatic, thyrotoxicosis, concomitant respiratory or renal disease, or other medically significant illness, which the investigator believes would be a

contraindication to study participation.
2. Significant concomitant respiratory disease such as cystic fibrosis, pulmonary fibrosis, aspergillosis, active or untreated primary tuberculosis.
3. Any significant abnormal laboratory results at screening, which in the opinion of the investigator, may put the subject at risk to take part in the study
4. Current diagnosis of asthma
5. Previous lung volume reduction surgery for the indication of COPD
6. Any use of home oxygen therapy
7. Patients with clinically significant laboratory abnormalities (not associated with the study indication) at screening
8. Recent acute exacerbation event requiring oral corticosteroids or antibiotics (any dose for more than 3 days) or respiratory tract infection 4 weeks prior to screening
9. History of active Malignancy in any organ system (diagnosis within last 12 months or ongoing active cancer treatment such as chemotherapy, radiotherapy, or immunotherapy.
10. History of treatment with biologics within four months or five half-lives (whichever is longer) prior to screening.
11. History of anaphylaxis to any biologic therapy or sensitivity of any component of IMP formulation
12. Have been involved in another medicinal trial (CTIMP) within the past 28 days
13. Women who are pregnant, lactating or intend to become pregnant during the study period
14. Planned surgical procedures requiring general anaesthesia or in-patient status for > 1 day during the conduct of the study.
15. Receipt of any live or attenuated vaccines within 15 days prior to screening
16. Patients whose treatment is considered palliative (life expectancy < 6 months).
17. History of chronic alcohol or drug abuse within 12 months prior to screening
18. Receipt of immunoglobulin or blood products within 30 days prior to screening
19. Use of immunosuppressive medication (e.g., methotrexate, troleandomycin, oral gold, cyclosporine, azathioprine, intramuscular long-acting depot corticosteroid) within 3 months prior to screening.
20. History of any known primary immunodeficiency disorder excluding asymptomatic selective immunoglobulin A or IgG subclass deficiency.
21. Subject taking antiretroviral medications, as determined by medical history
22. History of human immunodeficiency virus (HIV) or hepatitis B or C.

Date of first enrolment
29/02/2024

Date of final enrolment
30/01/2027

Locations

Countries of recruitment
United Kingdom

Denmark

Study participating centre

Glenfield Hospital
Groby Road
Leicester
England
LE3 9QP

Study participating centre
Kings College Hospital
Denmark Hill
London
England
SE5 9RS

Study participating centre
Bispebjerg Hospital
Bispebjerg Bakke 23
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Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type

Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

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?
Participant information sheet	version 3.0	22/11/2024	12/05/2025	No	Yes
Protocol file	version 3.0	22/11/2024	12/05/2025	No	No