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The effect on bacteria of breathing in (through an inhaler) a drug which reduces swelling (a steroid) in severe COPD (chronic obstructive pulmonary disease) patients with associated widening of the air tubes (bronchiectasis)

Submission date	**Recruitment status**	[X] Prospectively registered
23/02/2022	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
25/02/2022	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
10/12/2025	Respiratory	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

A key treatment for patients with advanced Chronic Obstructive Pulmonary Disease (COPD) is to optimise the airways using medicines to open the airways.

In patients with recurrent flare-ups, the addition of inhaled corticosteroids to reduce inflammation in the airways is recommended by national and international guidelines.

Recent published studies raised some concern that inhaled corticosteroids can promote chest infections including pneumonia. However, this is controversial, and the risks are uncertain.

We plan to perform a randomised controlled trial involving a high-risk group of severe COPD patients that have recurrent flare-ups due to bronchiectasis (associated widened and damaged airways) in 80 patients from 3 NHS hospital sites in Scotland. This patient group needs special attention as association of bronchiectasis in COPD can make them more prone to these exacerbations and can increase the mortality rate by up to 20-30%.

We aim to assess whether inhaled steroids along with other type of inhalers that open the airways can affect the amount and type of bacteria in the airways. This is a good patient group to test whether inhaled corticosteroids and other inhalers that open up the airways are safe and will improve patient symptoms and improve the burden of bacteria in lungs or not.

Who can participate?

Adults over 40 years, with COPD.

What does the study involve?

40 patients from each group will receive the dual inhaler ANORO ELLIPTA or the triple inhaler TRELEGY ELLIPTA (which includes the inhaled steroid) to determine the effect of the inhaled steroid over a variety of tests including a sputum test, breathing tests, amongst others. We will follow-up all participants for 12 months.

We also aim to look at the effect of oral corticosteroids on the bacteria in a small number of these patients (five from each treatment group). This would be very interesting and relevant as oral steroids are used for exacerbations in these high-risk patients.

What are the possible benefits and risks of participating?
The trial may not immediately benefit participants, but the results of the trial may change the practice of managing patients with COPD and Bronchiectasis in the future.
Patients recruited into TEMPESTAS will already be carefully managed by their clinical team due to their severe COPD. Following the washout period the patient will continue to use a daily inhaler and will be followed up. This will require the patient to respond to questions from sites around how they feel, collection of sputum samples, completion of an exacerbation diary and completion of questionnaires in order to collect data. This would cause minimal stress and inconvenience to the patient or be an intrusion to them.

Where is the study run from?
Not provided at time of registration

When is the study starting and how long is it expected to run for?
February 2022 to June 2025

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
Dr Gourab Choudhury, Gourab.Choudhury@nhslothian.scot.nhs.uk, TEMPESTAS.Trial@ed.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Dr Gourab Choudhury

Contact details
51 Little France Crescent
Edinburgh
United Kingdom
EH16 4TJ
+44 131 2422064
Gourab.Choudhury@nhslothian.scot.nhs.uk

Type(s)
Scientific

Contact name
Dr Gourab Choudhury

Contact details

51 Little France Crescent
Edinburgh
United Kingdom
EH16 4SA
+44 131 2422064
g.choudhury@ed.ac.uk

Type(s)
Public

Contact name
Dr Gourab Choudhury

Contact details
51 Little France Crescent
Edinburgh
United Kingdom
EH16 4SA
-
TEMPESTAS.Trial@ed.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2022-000524-38

Integrated Research Application System (IRAS)
1004221

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
AC21046, IRAS 1004221

Study information

Scientific Title
The microbial effect of inhaled steroids in severe COPD patients with associated bronchiectasis (TEMPESTAS)

Acronym
TEMPESTAS

Study objectives
In patients with severe COPD and bronchiectasis, does the addition of inhaled corticosteroids alter the microbial load of pathogens?

ICS beneficial effect would lead to an expected reduction in microbial load, with less significant bacterial loads (10 colony forming units/ml or more).

ICS detrimental effect, would lead to an expected increased microbial load, with significant bacterial loads (10 colony forming units/ml or more).

This would be assessed between the two groups (LABA-LAMA-ICS and LABA-LAMA arms).

Assess if ICS:
-Are beneficial, patients will have broadened microbial diversity in sputum microbiata and if detrimental there would be loss of this diversity
-Alter sputum colour, airways and systemic inflammation. The mechanism of inhaled corticosteroids is anti-inflammatory, and hypothesis is that inhaled corticosteroids might improve sputum colour, reduce sputum and serum inflammation
-Impact on microbial and mycobial community composition
-Impact on spirometry (forced expired volume in 1 second, forced vital capacity, its ratio and mid expiratory flows FEF25-75)
-Impact on health status using well-validated quality of life questionnaires in bronchiectasis
-Moderate/ severe exacerbation rate and time to first moderate/ severe exacerbation
-if addition of inhaled corticosteroid has an overall beneficial/detrimental effect to the mortality rate and whether that correlates with microbial diversity that is being assessing in these 2 groups

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/05/2022, North West - Greater Manchester Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 207 1048 007; gmcentral.rec@hra.nhs.uk) ref: 22/NW/0079

Study design
Interventional open label randomized parallel group controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease (COPD) with widening of the air tubes (bronchiectasis)

Interventions
This is an open label randomised trial. 80 patients with COPD and coexistent bronchiectasis to be recruited with 40 patients in each arm. one arm would receive triple therapy of inhalers (inhaled corticosteroids(ICS)/Long acting beta agonist/Long acting antimuscarinic) and the other dual bronchodilator (Long acting beta agonist/Long acting antimuscarinic) to assess the effect of ICS on microbial architecture (microbial load, microbiome and mycobiome heterogenity) in this group of patients. Randomisation will be done by an online tool centrally from Edinburgh. Patients will be offered the treatment for 12 months after an initial washout period of a month with the dual bronchodilator in both the groups. As a tertiary endpoint 5 patients from each arm at the end of the main study will receive a week of oral prednisolone to assess if oral corticosteroids further has an effect on the endpoints assessed with the ICS for the main study.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
ANORO ELLIPTA inhaler: 55/22, (combination of umeclidinium 55mcg and vilanterol 22mcg), TRELEGY ELLIPTA inhaler: 92/55/22 (combination of umeclidinium 55mcg vilanterol 22mcg and fluticasone furoate 92mcg)

Primary outcome(s)
A baseline to 1-year change (expressed in log units) in colony forming units per ml between treatment arms (LABA-LAMA plus corticosteroid versus LABA-LAMA only) measured via sputum samples taken at baseline, 6 months & 12 months between the 2 arms of the study.

Key secondary outcome(s))
1. Change in sputum microbial diversity and microbial biomass (see analyses below for details) between the two arms. measured via sputum samples taken at baseline, 6 months & 12 months
2. Sputum colour as assessed by a standardised colour chart- patients are graded as mucoid (clear or grey phlegm, muco-purulent (light yellow or green) and purulent (dark yellow or green) measured via sputum samples taken at baseline, 6 months & 12 months
3.1. Microbial community composition (gram negative/positive ratio, abundance of potential pathogens etc.) measured via sputum samples taken at baseline, 6 months & 12 months
3.2. Fungal microbiome: between the two groups to see if ICS can influence the heterogeneity of the fungal community in terms of absolute and relative abundance. measured via sputum samples taken at baseline, 6 months & 12 months
4. Spirometry: forced expired volume in 1 second, forced vital capacity and its ratio and mid expiratory flows (FEF25-75) (attenuation of decline in lung function would be of long-term benefit to patients if found). Measured using spirometry at screening and consenting visit, baseline, 6 months & 12 months
5. Quality of Life: quality of life assessed by the COPD Assessment Tool (CAT) and St. Georges Respiratory Questionnaire. Breathlessness is included as part of this questionnaire. Questionnaires completed at baseline, 6 months & 12 months and at exacerbation visits
6. Sputum inflammation: we will assess sputum myeloperoxidase as a measure of neutrophil burden and free elastase activity. measured via sputum samples taken at baseline, 6 months & 12 months
7. Serum inflammation: we will measure white cell count and differential, erythrocyte sedimentation rate (ESR), C Reactive Protein (CRP) and intercellular adhesion molecule 1 (ICAM-1) Previous research has shown that at high bacterial loads there is increased ICAM-1 Measured via blood tests at baseline, 6 months & 12 months
8. Exacerbations: These would be categorised as *time to the first exacerbation requiring treatment with antibiotics and/steroids, *number of exacerbations (needing antibiotics and /steroids) over 12 months including hospitalisations *number of participants with radiologically confirmed pneumonia over this period. Patient provided with diary to report all exacerbations. Diaries reviewed at baseline, 1month, 6 months, 12 months, 12 months + 7days
9. Mortality rate between the 2 arms of the study groups. Considering the group's overall but also separately broken down by microbe and microbial diversity.
10. Safety endpoints:
The incidence of all AE and SAE across both treatment arms would be described as well as a safety endpoint.

To assess and investigate safety and benefits of a trial design like this, we will also document parameters such as respiratory failure), hospitalized exacerbations (along with other exacerbation data as specified above), and trial dropout due to worsening COPD symptoms as safety endpoints. This would be documented between both the arms of the study. Collection of all AE & SAE data at baseline, 1month, 6 months, 12 months, 12 months + 7days

Completion date
30/06/2025

Eligibility

Key inclusion criteria
Subjects eligible for enrolment in the study must meet all of the following criteria:
1. Informed Consent: A signed and dated written informed consent prior to study participation.
2. Type of subject: Outpatient.
3. Age: Subjects 40 years of age or older at screening visit.
4. Gender: Male or female subjects.
5. COPD Diagnosis: An established clinical history of COPD as documented in medical notes in accordance with the definition by the American Thoracic Society/European Respiratory Society. COPD-Bronchiectasiscoexistence: smoking history of greater than 10 pack year, with a post bronchodilator FEV1/FVC ratio <0.7 with coexistent bronchiectasis on a high-resolution CT Chest (increased broncho-arterial ratio in two or more lobes of the lung). CT scans would have been done prior to recruitment as a part of usual clinical pathway.
5.1 Two or more exacerbations in the last 1-year (requiring antibiotics and/steroids) or one or more hospitalisation in accordance with GOLD D (2017) classification (high risk more symptom COPD patients) but clinically stable during screening period.
5.2 Clinically stable is defined as not requiring antibiotics and or steroid 4 weeks prior to study entry. This will be checked during the randomisation visit from patient history and documented by the research nurses.
6. Smoking history: Current or former cigarette smokers (cigarettes or rolled tobacco) with a history of cigarette smoking of >10 pack-years at screening (visit 1) [number of pack years = (number of cigarettes per day / 20) x number of years smoked (e.g., 20 cigarettes per day for 10 years, or 10 cigarettes per day for 20 years)]. Previous smokers are defined as those who have stopped smoking for at least 6 months prior to Visit 1. Note: Pipe and/or cigar use cannot be used to calculate pack-year history.

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. Pregnancy: Women who are pregnant or breast feeding or are planning on becoming pregnant during the study.
2. Asthma: Subjects with a current/ concurrent diagnosis of asthma.
3. α1-antitrypsin deficiency: Subjects with known α1-antitrypsin deficiency as the underlying cause of COPD.
4. Other respiratory disorders: Subjects with active tuberculosis, active lung cancer, sarcoidosis, lung fibrosis, pulmonary hypertension, or other interstitial lung diseases.
5. Lung resection: Subjects with lung volume reduction surgery within the 12 months prior to Screening.
6. Risk Factors for Pneumonia: immune suppression (e.g. HIV, Lupus) or other risk factors for pneumonia, when patients are on long standing immunosuppressive drugs or have neuromuscular conditions affecting control of the upper airway, such as Parkinson's disease, Motor Neuron Disease or Myasthenia Gravis.
7. Pneumonia and/or moderate or severe COPD exacerbation that has not resolved at least 14 days prior to Screening and at least 30 days following the last dose of oral/systemic corticosteroids (if applicable). In addition, any subject that experiences pneumonia and/or moderate or severe COPD exacerbation during the washout period will be excluded.
8. Other Respiratory tract infections that have not resolved at least 7 days prior to screening including COVID19 infections
9. Other diseases/abnormalities: Subjects with historical or current evidence of any of the following clinically significant abnormalities that are uncontrolled:
9.1. cardiovascular
9.2. neurological
9.3. psychiatric (including documented psychiatric reactions or hypersensitivity to oral steroids)
9.4. renal
9.5. hepatic
9.6. immunological
9.7. gastrointestinal
9.8. urogenital (e.g. significant prostatic hyperplasia/bladder outflow obstruction)
9.9. nervous system
9.10. musculoskeletal (including known significant osteoporosis)
9.11. skin
9.12. sensory
9.13. endocrine (including uncontrolled Type 1 or 2 diabetes or thyroid disease)
9.14. ocular (e.g. significant narrow angle glaucoma)
9.15. haematological
10. Unstable liver disease as defined by the presence of ascites, encephalopathy, coagulopathy, oesophageal or gastric varices or persistent jaundice.
11. Unstable or life-threatening cardiac disease
12. Abnormal and clinically significant 12-Lead ECG finding
13. Other Contraindications: A history of allergy or hypersensitivity to any oral steroid or corticosteroid, anticholinergic/muscarinic receptor antagonist, beta2-agonist, lactose/milk protein or magnesium stearate or a medical condition such as narrow-angle glaucoma, uncontrolled symptomatic prostatic hypertrophy or bladder neck obstruction that, in the

opinion of the Investigator contraindicates study participation.
14. Cancer: Subjects with carcinoma that has not been in complete remission for at least 5 years. Subjects who have had carcinoma in situ of the cervix, prostrate carcinoma, squamous cell carcinoma and basal cell carcinoma of the skin would not be excluded based on the 5year waiting period if the subject has been considered cured by treatment.
15. Oxygen therapy: Use of long-term oxygen therapy (LTOT) described as resting oxygen therapy >3L/min (Oxygen use up to 3L/min flow is not exclusionary.)
16. Medication prior to spirometry: Subjects who are medically unable to withhold their salbutamol for the 4-hour period required prior to spirometry testing at each study visit.
17. Pulmonary rehabilitation: Subjects who have participated in the acute phase of a Pulmonary Rehabilitation Program within 4 weeks prior to Screening or subjects who plan to enter the acute phase of a Pulmonary Rehabilitation Program during the study. Subjects who are in the maintenance phase of a Pulmonary Rehabilitation Program are not excluded.
18. Drug/alcohol abuse: Subjects with a documented known or suspected history of alcohol or drug abuse within the last 2 years.
19. Non-compliance: Subjects at risk of non-compliance, or unable to comply with the study procedures. Any infirmity, disability, or geographic location that would limit compliance for scheduled visits. Non-compliance with requirement for adherence to at least 50% compliance with washout medication, verified at visit 2. Non-compliance with requirement for adherence to at least 50% compliance with trial medication, verified at visit 5.
20. Inability to read or write English.
21. Medication prior to screening: Use of the following medications within the following time intervals prior to Screening (Visit 1) or during the study:
Systemic, Oral, parenteral Corticosteroids - 30 days (Except during the study oral/systemic corticosteroids may be used to treat COPD exacerbations/pneumonia Intra-articular injections are allowed.
Any other investigational drug -30 days
22. Suspected atypical infection.
23. Already enrolled in another study.

Date of first enrolment
16/05/2022

Date of final enrolment
30/09/2023

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian

Scotland
EH16 4SA

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
Scotland
G4 0SF

Study participating centre
Victoria Hospital
Hayfield Road
Kirkcaldy
Scotland
KY2 5AH

Sponsor information

Organisation
The University of Edinburgh & Lothian Health Board

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

Following publication, anonymised patient level data and samples from the Study may be shared with other researchers on reasonable request in writing to the Chief Investigator. Gourab.Choudhury@nhslothian.scot.nhs.uk
Potential participants will be informed of this and will provide their consent.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			20/09/2023	No	No
Other files	Participant flow, baseline characteristics, adverse events	01/12/2025	10/12/2025	No	No
Protocol file	version 5.0	02/05/2024	10/12/2025	No	No
Statistical Analysis Plan	version 2.1	21/07/2025	10/12/2025	No	No
Study website		11/11/2025	11/11/2025	No	Yes