ISRCTN70034823 https://doi.org/10.1186/ISRCTN70034823

GREAT-2: a trial of gremubamab compared to placebo in participants with bronchiectasis and chronic Pseudomonas aeruginosa infection

Submission date
15/11/2022

Recruitment status
No longer recruiting

Registration date
26/05/2023

Overall study status
Completed

Last Edited
04/07/2025

Condition category
Respiratory

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Patients with bronchiectasis often get chest infections which are difficult to treat causing coughing, sputum (phlegm) production, breathlessness and tiredness. Approximately one third of people with bronchiectasis become infected with bacteria called Pseudomonas aeruginosa (P. aeruginosa). P. aeruginosa can often become resistant to antibiotics. The purpose of this trial is to test whether an intravenous infusion (drip) containing a new drug called gremubamab can reduce the amount of infection with P. aeruginosa.
The purpose of this trial is to test whether a new drug called gremubamab, given intravenously, can reduce the amount of infection with P. aeruginosa in people with bronchiectasis. Whether gremubamab can help reduce the number of bronchiectasis exacerbations and improves quality of life will also be examined. The safety of gremubamab use in people with bronchiectasis will be assessed.
Gremubamab is a type of drug called a monoclonal antibody which is expected to work with the immune system to eliminate the P. aeruginosa infection.
Gremubamab is a new medication which is being developed by AstraZeneca. It has been used in a few trials already, in healthy people (Phase I trial) and people who were on a ventilator in intensive care and developed pneumonia (Phase II trial). Phase I trials look at the safety of new drugs and phase II trials look at how effective new drugs are as well as their safety. This trial is a phase II trial which will look at the safety and effectiveness of gremubamab in people with bronchiectasis.

Who can participate?
People aged 18 – 85 years with bronchiectasis in the UK and Spain

What does the study involve?
The health of participants treated with gremubamab will be compared with the health of participants given a placebo. The effects of two different doses will also be compared.
The participant will be in the trial for 6 months and will receive infusions of the gremubamab /placebo at monthly intervals for the first 3 months. The trial is expected to run for a total of 18 months.

What are the possible benefits and risks of participating?
Benefits:
Participants will be monitored closely during the trial by the trial team. The tests will give the trial team information about the function of participants kidneys, liver, fitness and general wellbeing. If any of these investigations reveal any new clinically significant abnormality, the trial team will tell participants and either discuss this with their GP (with your consent) or refer them to a specialist clinic at the hospital (whichever seems most appropriate.) The trial may not immediately benefit participants, but if the results of the trial are positive this may improve how people with bronchiectasis are treated.
Risks:
Previous trials have shown that there was a low risk of allergic reactions to the gremubamab infusion. There is an extremely small risk of severe allergic reaction. The risk of having an allergic reaction will be reduced by giving the infusion slowly and giving an antihistamine before the trial drug administration starts. Participants will be monitored during all infusions of trial medication. A participant's trial medication will be stopped immediately a participant develops signs of a severe allergic reaction.
A few people in the previous trials also reported headache, indigestion and itch.
If a participant develops any reaction to the infusion the doctor looking after the participant will assess it and discuss with the participant if any treatment is required. The doctor will also decide if it is suitable for the participant to continue with their infusions.

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

When is the study starting and how long is it expected to run for?
November 2022 to October 2024

Who is funding the study?
European Respiratory Society (UK)

Who is the main contact?
Dr James Chalmers, j.chalmers@dundee.ac.uk

Contact information

Type(s)
Public

Contact name
Dr Gillian Martin

Contact details
Tayside Clinical Trials Unit
TASC
Level 3, Ninewells Hospital and Medical School
Dundee
United Kingdom
DD1 9SY
+44 (0)1382 381955
GREAT-2-TM@dundee.ac.uk

Type(s)
Principal investigator

Contact name
Dr James Chalmers

ORCID ID
https://orcid.org/0000-0001-5514-7868

Contact details
Ninewells Hospital and Medical School
Dundee
United Kingdom
DD1 9SY
+44 1382 386131
j.chalmers@dundee.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2022-003215-28

Integrated Research Application System (IRAS)
1005993

Central Portfolio Management System (CPMS)
55567

Protocol serial number
1-023-22

Study information

Scientific Title
GRemubamab ErAdication Trial (GREAT-2) A phase 2 trial of gremubamab compared to placebo in participants with bronchiectasis and chronic Pseudomonas aeruginosa infection

Acronym
GREAT-2

Study objectives
Primary objective:
To evaluate the efficacy of gremubamab on P. aeruginosa bacterial burden in sputum at week 12

Secondary objectives:
1. To evaluate the efficacy of gremubamab on P. aeruginosa bacterial burden in sputum
2. To determine the persistent effects of gremubamab on P. aeruginosa bacterial burden following discontinuation of treatment (week 24)
3. To determine if gremubamab can achieve eradication of P. aeruginosa in some individuals
4. To determine the effect of gremubamab on health related quality of life

5. To determine the effect of gremubamab on time to first exacerbation
6. To determine the effect of gremubamab on pulmonary function
7. To assess the safety of gremubamab in patients with bronchiectasis
8. To evaluate the PK of gremubamab

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/05/2023, East of Scotland Research Ethics Service (EoSRES, Tayside Medical Science Centre, Residency Block, Level 3, George Pirie Way, Dundee, DD1 9SY, UK; +44 (0)1382 383871; tay.eosres@nhs.scot), ref: 22/ES/0051

Study design
Interventional double-blind randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Bronchiectasis

Interventions
Participants will be randomised using a GCP-compliant Interactive Web-based Randomisation System to one of three treatment arms. Randomisation will be stratified by inhaled antibiotic use. Depending on randomisation participants will receive either gremubamab 1500 mg per dose, gremubamab 500 mg per dose or placebo. Participants will receive trial treatment via intravenous infusion every 4 weeks a total of three times. Participants will be assessed during the treatment period (3 months) and for a 3-month period following completion of trial treatment.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Efficacy of gremubamab on P. aeruginosa bacterial burden in sputum measured by change from baseline (day 1 - day 84) in quantitative sputum cultures (colony-forming unit (CFU))

Key secondary outcome(s))
1. Efficacy of gremubamab on P. aeruginosa bacterial burden in sputum measured by change from baseline to Days 7, 14, 28 and 56 in Quantitative sputum cultures
2. Persistent effects of gremubamab on P. aeruginosa bacterial burden following

discontinuation of treatment measured by change from baseline to Day 168 in quantitative sputum cultures
3. Eradication defined by negative sputum cultures for P. aeruginosa at the end of treatment (Days 84 and 168)
4. Eradication of P. aeruginosa of measured by change from baseline to Days 28, 56, 84 and 168 in QOL-B, BIM questionnaire
5. Effect of gremubamab on health-related quality of life
5.1. Measured by change from baseline to Days 84 and 168 in St. George's Respiratory Questionnaire
5.2. Measured by change from baseline to Days 28, 56, 84 and 168 in change from baseline in Quality of Life Bronchiectasis questionnaire
5.3. Measured by change from baseline to Days 28, 56, 84 and 168 in change from baseline in Bronchiectasis Impact Measure questionnaire
6. Effect of gremubamab on time to first exacerbation measured by occurrence of exacerbations (as per EMBARC definition of exacerbation). First event from visit 1 to day 84.
7. Effect of gremubamab on pulmonary function measured by change from baseline to Day 28, 56 and 84 in forced expiratory volume in 1 second (FEV1)
8. Safety of gremubamab in patients with bronchiectasis measured by frequency of adverse events and serious adverse events between groups over 168 days
9. Safety of gremubamab in patients with bronchiectasis measured by safety lab parameters between groups over 168 days
10. Pharmacokinetics of gremubamab measured by gremubumab PK parameters through 168 days post-dose

Completion date
31/10/2024

Eligibility

Key inclusion criteria
1. Age 18 ≤ 86 years
2. Clinical diagnosis of bronchiectasis.
3. Able to and provided informed consent.
4. Previous CT scan of the chest demonstrating bronchiectasis in 1 or more lobes
5. P. aeruginosa in sputum, bronchoalveolar lavage or another airway sample at least once in the 24 months prior to screening.
6. A sputum sample that is culture positive for P. aeruginosa sent at the screening visit and within 35 days of randomization.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
86 years

Sex
All

Total final enrolment
62

Key exclusion criteria
1. Known hypersensitivity to gremubamab or any excipient of the investigational product
2. Known clinical diagnosis of cystic fibrosis
3. Immunodeficiency requiring replacement immunoglobulin.
4. Active tuberculosis or nontuberculous mycobacterial infection (currently under treatment, or requiring treatment in the opinion of the investigator).
5. Active allergic bronchopulmonary aspergillosis (receiving treatment with corticosteroids and /or antifungal medication).
6. Recent significant haemoptysis (a volume requiring clinical intervention, within the previous 4 weeks prior to screening).
7. Treatment with long-term inhaled, systemic or nebulized anti-pseudomonal antibiotics which are newly initiated within the previous 3 months prior to screening.
8. Chronic treatment with cyclical doses of inhaled or nebulized antibiotics e.g. 28 days on and 28 days off at the time of screening.
9. Receipt of antipseudomonal antibiotics for an exacerbation during the screening period.
10. Treatment with immunosuppressives within previous 6 months prior to screening.
11. Participants with a primary diagnosis of COPD associated with >10 pack years smoking history.
12. Participants with a primary diagnosis of asthma or asthma which is considered to be poorly controlled at screening.
13. Participants with FEV1 <25% predicted value at screening.
14. Glomerular filtration rate (eGFR) below 25 ml/min/1.73m² or requiring dialysis. This will be determined at screening.
15. Use of any investigational drugs within five times of the elimination half-life after the last dose or within 30 days, whichever is longer.
16. Unstable co-morbidities (e.g. cardiovascular disease, active malignancy) which in the opinion of the investigator would make participation in the trial not in the participant’s best interest.
17. Pregnant or lactating females.
18. Women of child baring age or male partners of women of childbearing age and not practicing a method of acceptable birth control

Date of first enrolment
10/08/2023

Date of final enrolment
24/01/2024

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Spain

Study participating centre
Ninewells Hospital and Medical School
NHS Tayside
Ninewells Avenue
Dundee
United Kingdom
DD1 9SY

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
University Hospital Llandough
Penlan Road
Llandough
Penarth
United Kingdom
CF64 2XX

Study participating centre
Royal Brompton Hospital
Sydney Street
London
United Kingdom
SW3 6NP

Study participating centre

Royal Papworth Hospital
Papworth Road
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0AY

Study participating centre
Hammersmith Hospital
Du Cane Road
Hammersmith
London
United Kingdom
W12 0HS

Study participating centre
Royal Devon and Exeter Hospital
Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
The Princess Alexandra Hospital
Hamstel Road
Harlow
United Kingdom
CM20 1QX

Study participating centre
Belfast City Hospital
51 Lisburn Rd
Belfast
United Kingdom
BT9 7AB

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe

Manchester
United Kingdom
M23 9LT

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Study participating centre
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Sponsor information

Organisation
University of Dundee

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Research organisation

Funder Name
European Respiratory Society

Alternative Name(s)
ERS

Funding Body Type

Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to commercial sensitivity.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		24/06/2025	04/07/2025	No	No
HRA research summary			20/09/2023	No	No
Other files	version 3	29/09/2023	26/01/2024	No	Yes
Participant information sheet	version 1	10/11/2022	17/11/2022	No	Yes
Participant information sheet	version 2	05/05/2023	26/05/2023	No	Yes
Participant information sheet	version 3	29/09/2023	26/01/2024	No	Yes
Participant information sheet	version 2	05/05/2023	26/01/2024	No	Yes
Protocol file	version 4	19/10/2023	06/12/2023	No	No
Protocol file	version 5	13/12/2023	26/01/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes