

PARTICIPANT INFORMATION SHEET

GREAT-2 – GRemubamab ErAdication Trial Gremubamab compared to placebo in participants with bronchiectasis and chronic *Pseudomonas aeruginosa* infection

Chief Investigator

Professor James Chalmers

We are inviting you to take part in a research trial

Before you choose whether or not to take part, we want you to understand why we're doing this trial. We also want you to know what will be involved if you agree to take part. Please take time to read this information carefully. You can ask us any questions you have and talk to other people if you want. We'll do our best to answer your questions and give you any more information you ask for. You don't have to decide straight away.

Why have I been contacted?

We are inviting you to take part because you have bronchiectasis and have had an infection caused by *P. aeruginosa* in the last 2 years. A total of 90 participants in the UK and in Spain will take part in the trial.

If you have had antibiotics started in the last 3 months, you will not be able to take part. However, if you are taking long-term antibiotics and changes are not expected then you should be able to take part. The research doctor will check this with you.

The doctor will also check to see if there are any other reasons why the trial would not be suitable for you. .

You will not be able to take part if you are pregnant, breastfeeding or planning a pregnancy.

Why are we doing this trial?

Patients with bronchiectasis frequently get chest infections which are difficult to treat and can cause coughing, sputum (phlegm) production, breathlessness and tiredness. Approximately one third of people with bronchiectasis become infected with a bacteria called *Pseudomonas aeruginosa* (*P. aeruginosa*). *P. aeruginosa* often becomes resistant to antibiotics which means antibiotics don't work. People are often left with a chronic infection which is difficult to treat. Having a chronic infection with *P. aeruginosa* may lead to you being more likely to be admitted to hospital, may also increase your risk of more serious illness.

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*. We'll also assess whether people with bronchiectasis can take this drug safely. We will also look to see if Gremubamab reduces the number of bronchiectasis exacerbations and improves quality of life.

Gremubamab is a type of drug called a monoclonal antibody which we hope will work with your 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.

What is being tested?

We will compare the health of participants treated with Gremubamab with the health of participants given a placebo, which is a substance that looks the same as Gremubamab but is not an active medicine (dummy medicine). You won't be able to choose whether you receive the Gremubamab medicine or the placebo medicine, this will be decided in a random way (a bit like tossing a coin but done by a computer). Neither you, your nurse nor your doctor will be told if you will receive the Gremubamab or placebo. You will not be able to ask to find this out, but we'll tell you once the trial is finished and the results of the trial are published. In an emergency, if a doctor looking after you needs to know what treatment you are receiving for your safety, they will be able to request this information.

We will also compare the effects of two different doses of the medicines. Half the participants will be given a higher dose than the rest. This will be decided randomly and neither you, your nurse nor your doctor will be told what dose you are prescribed until after the trial is complete.

You will be given the Gremubamab or placebo infusion once per month for 3 months. To take part in the trial you'll have to be happy to receive either the Gremubamab medication or the placebo medication, and to receive either the lower dose or the higher dose of medication.

Do I have to take part?

No. Taking part in this trial is entirely up to you. If you choose to take part, you can stop the trial at any time. You don't have to give a reason for not taking part or for stopping, and the medical care you get and your relationship with the medical or nursing staff looking after you won't be affected. However, if you are happy to tell us, we would find it useful to know the reason for not taking part, so that we can look at ways of improving the trial and future trials.

What will happen to me if I take part?

You will be in the trial for approximately 6 months which will involve you attending hospital for 8 appointments during that time. If you have an exacerbation of your bronchiectasis during the trial, you'll attend for an extra visit to assess your symptoms. This does not mean that you would necessarily have to stop the trial treatment.

Visit 1

The first appointment is a screening visit where we'll carry out assessments to confirm whether the trial is suitable for you. This visit will take around 2 hours. We'll ask you to complete a consent form to confirm that you wish to take part in the trial. We'll give you a physical examination and ask about your medicines and illnesses and check your medical notes. We'll then carry out a number of procedures:

- Pulse and blood pressure
- Height and weight
- Temperature
- Oxygen levels – a painless clip is attached to your finger to measure the amount of oxygen in your blood
- ECG (electrocardiogram) – a tracing of your heart rate

- Blood test – we'll take around 50ml (3 tablespoons)
- Sputum sample – you'll be asked to produce a sputum sample that we'll test for *P. aeruginosa*. If you cannot produce a sample, we'll ask you to attend the hospital again within the next week. You can bring a fresh sputum sample with you if you find it difficult to produce a sample at the hospital. If *P. aeruginosa* is not found, you'll be able to bring another sample during the next 3 weeks to see whether *P. aeruginosa* is present.
- Spirometry – after you have been given the short-acting bronchodilator called salbutamol (either with a nebuliser or with an inhaler), you'll be asked to breathe quickly and forcefully into a mouthpiece. The mouthpiece is attached to a machine which measures how much air you can breathe out in one forced breath. If you have your own salbutamol inhaler, please bring it to your appointment and you can use that.
- Questionnaires – you'll be asked to complete questionnaires which will assess how troublesome your bronchiectasis is and how it impacts on your quality of life.
- Pregnancy test (blood) – for women of childbearing age.

Treatment phase

If your sputum shows you have *P. aeruginosa* infection and other test results confirm that the trial is suitable for you, you'll be invited to join the trial and will be asked to come for your next visit. If you do not have *P. aeruginosa* you will not be able to take part in the trial, unless you develop it at a later date.

Visit 2

Within 35 days of your first visit, you'll attend your second visit. This visit will take around 5 hours. You'll have the following assessments:

- Pregnancy test (urine)– for women of childbearing age.
- Sputum sample

- Blood test – we'll take around 50ml (3 tablespoons)
- Antihistamine – we'll give you antihistamine medication before you receive your trial medication. This is to reduce the chance of an allergic reaction to the trial medication.
- Trial medication - You'll receive the first intravenous infusion of the trial medication. This will take around 4 hours. During the infusion your blood pressure, pulse and oxygen levels will be checked regularly.
- Questionnaires – you'll be asked to complete 3 questionnaires which will assess how troublesome your bronchiectasis is and how it impacts on your quality of life.

Visits 3 and 4

You'll come back after 1 week and again after 2 weeks. At these visits you'll be asked about your health and any changes to your normal medications. You'll also have the following assessments:

- Blood pressure, pulse, temperature and oxygen saturation
- Blood test – around 50ml (3 tablespoons)
- Sputum sample
- Questionnaires
- Pregnancy test – if appropriate

Visits 5 and 6

At both 4 weeks and 8 weeks after your first infusion you will come back for further infusions, each lasting around 4 hours. You'll have the same procedures as at visit 2.

Visit 7

This will be 1 month after your third (last) trial infusion. This will be the same procedures as visits 3 and 4.

- Blood sample – around 50ml

Telephone call

2 months after your last infusion we will phone you to ask about your health and any changes to your medications.

Visit 8

You'll be asked to come back 3 months after your last infusion for your final visit. This will be the same procedures as visits 3 and 4

- Blood sample –around 50ml

What will my blood and sputum samples be used for?

During the trial blood and sputum samples will be collected at different visits. These will be collected for the following reasons.

Blood samples:

- Safety blood samples: to check that your liver, kidney and other organs are working well.
- Biomarker blood samples: for the research lab to check markers of lung inflammation.
- Genetic blood test: to allow researchers to learn about differences and changes in an individual's genetic makeup, which may help to discover the role that genetics play in disease and treatment. The genetic tests are done only for research and will not be useful for your clinical care you will not get the results of any of these tests.
- Pharmacokinetics (PK) and anti-drug antibodies (ADA) analysis: to examine what the body does when given Gremubamab for example, how long it takes to absorb the medication and how long it stays in the body. These samples will also be taken before and after you receive your trial medication at visits 2, 5 and 6. These tests will only be carried out if the results of the trial indicate that Gremebamab helps people with Bronchiectasis.

- If you agree, we will also take additional blood samples and store them so researchers can use them in the future for clinical research. Some of these samples may be used for genetic analysis to identify inherited factors that influence the development of disease. These additional samples are optional, and you can still take part in the trial if you don't want to give these extra samples.

Sputum samples

- *P. aeruginosa*: at the screening visit we will check to see if you have *P. aeruginosa* in your sputum to determine if you are able to take part in the trial. At later visits we will check the levels of *P. aeruginosa* to see if they are changing.
- Biomarker sputum samples: for the research lab to check markers of lung inflammation.
- If you agree, we will also take an additional sputum sample and store it so researchers can use it in the future for clinical research. This is optional and you can still take part in the trial if you don't want to give this extra sample.

Will taking part in the trial affect my usual care?

No, you'll continue to receive your usual care including taking any medications which you normally take.

We will ask your GP to not prescribe new long-term oral or inhaled antibiotics when you are in the trial unless you are already taking these before joining the trial and oral anti-pseudomonal antibiotics. Antibiotics may be prescribed if you have an acute exacerbation.

You should not donate blood during while you are in the trial.

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Phone call	Visit 8	Extra visits
	Screening	Start	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16	Week 24	If required
Consent form	X									
Health & medication check	X	X	X	X	X	X	X	X	X	X
Physical examination	X									X
ECG	X									
Blood pressure, pulse, temperature and oxygen saturation	X	X	X	X	X	X	X		X	X
Pregnancy test (if applicable)	X	X			X	X			X	
Blood samples	X	X	X	X	X	X	X		X	X
Sputum samples	X	X	X	X	X	X	X		X	X
Spirometry	X				X	X	X		X	
Questionnaires	X	X		X	X	X	X		X	X
Antihistamine		X			X	X				
Trial medication		X			X	X				

What will happen when the trial finishes?

The trial drug will not be available after the end of the trial, so you won't receive the trial medication when the trial finishes. If the trial gives an indication of possible benefit from the medicine being tested it is likely that more trials with larger numbers of participants will be needed. It could be some time before we're sure about how useful Gremubamab is for people with bronchiectasis.

We hope to finish the trial in early 2024 but it may take a up to a year before we can publish the results. We will send you a letter with the results once we have them. We will also let you know if you received the Gremubamab or the placebo at that point.

If Gremubamab is found to be useful for people with bronchiectasis it is likely that it will be given by infusion. We may need to do more trials to see what the best way to prescribe it would be.

What are the possible benefits of taking part?

You'll be monitored closely during the trial by the trial team. The tests will give us information about the function of your kidneys, liver, your fitness and general wellbeing. If any of these investigations reveal any new clinically significant abnormality, we'll tell you and either discuss this with your GP (with your consent) or refer you to a specialist clinic at the hospital (whichever seems most appropriate.) The trial may not immediately benefit you, but if the results of the trial are positive this may improve how we treat people with bronchiectasis just like you.

What are the possible disadvantages and risks of taking part?

These trials showed that there was a low risk of allergic reactions to the Gremubamab infusion. There is an extremely small risk of severe allergic reaction. We will reduce the risk of you having an allergic reaction by giving the infusion slowly and giving you an antihistamine through your infusion before your medication starts. You'll be monitored during all infusions of trial medication. The trial medication will be stopped immediately if you have signs of a severe allergic reaction.

A couple of people in the previous trials also reported headache, indigestion and itch.

If you develop any reaction to the infusion the doctor looking after you will assess it and discuss with you if any treatment is required. The doctor will also decide with you if it is suitable for you to continue with your infusions.

Contraceptive advice

All women who could get pregnant must have a pregnancy test at the visit before you take the trial medication and at the end of the trial. If you are a woman who could get pregnant, and you are sexually active with a man you must be willing to use a birth control method which is medically approved during this trial.

If you are a man and are sexually active with a woman who could get pregnant you must be willing to use a birth control method which is medically approved during this trial.

Medically approved birth control:

- Combined or progesterone only hormonal contraception e.g. pill, injection, implant or patch
- Intrauterine device – 'coil'

- Female sterilisation
- Male partner vasectomy – sterilisation

If you or your partner does get pregnant during the trial, please tell us and we'll follow your health and the health of the baby during pregnancy and at birth.

What will happen if I want to stop the trial medication or don't want to carry on with the trial?

If you develop any concerns over participating in the trial, please talk to us to discuss these concerns and the different options available to you.

It is important for us to get as much data as possible for the results of the trial to be reliable. If either you or the trial doctor stops the trial medication, continuing to attend the trial visits and completing the assessments will help make sure the results of the trial are as useful as possible.

You are free to withdraw from the trial at any time without providing a reason. However, we would find it useful to know the reason for withdrawal, this may help us improve this trial and future trials. If you want to stop the trial, all medical care you get and your relationship with the medical or nursing staff looking after you won't be affected. All personal identifiable data can be withdrawn, should you request it.

Will I receive any payment for taking part?

You won't receive any payment for taking part, but you will receive taxi transport or reasonable travel expenses to attend the research visits. For the longer visits (visits 2, 5 and 6) you will also receive refreshments and something to eat.

Who is organising and funding this research?

This trial is being sponsored by the University of Dundee and NHS Tayside. It is being funded by the European Respiratory Society and the Gremubamab and placebo treatments are being provided free of charge by AstraZeneca. The trial is being organised by Professor James Chalmers.

The researchers and your doctor will not receive any personal payment for your participation in the trial. Your hospital will only receive payment to cover the costs of your participation.

How have patients and the public been involved in the trial?

The design of the trial and many of the procedures being carried out, such as the questionnaires, have been developed with feedback from a group of people with bronchiectasis working with a patient organisation called the European Lung Foundation. The trial has been developed partly because patients have told us that they would like treatments for bronchiectasis that tackle the problem of chronic infection of *P. aeruginosa*.

What COVID-19 precautions will be in place when I come for my visits?

The current local COVID-19 guidelines will be in place when you come for your visits. This may include wearing facemasks, handwashing, social distancing when appropriate, checking your temperature and asking about any recent COVID-19 symptoms.

Staff will wear face masks and other personal protective equipment (PPE) when appropriate. Social distancing will be in place when possible.

What will happen with the information collected about me?

Identifiable information about you and the information collected about you during the trial will be stored by your local NHS research team either on paper or on their local NHS computers. Only certain members of the research team can access this information.

People who don't need to know who you are won't be able to access your name or contact details. Your data will have a code number instead. Only certain members of your local research team will have the link between your code number and your personal information.

Information collected about you during the trial is called "trial information". Your trial information will be securely stored on password protected databases in the University of Dundee.

Your trial information will be kept securely for 25 years after the end of the trial. This is a legal requirement for trials using medication. After 25 years your identifiable information will be removed, and the rest of the information will be kept for research purposes. If you'd like to be informed about future trials that you might be interested to participate in, we'll ask you to sign a consent to allow your local research team to hold your contact details.

We'll ask your permission to tell your GP that you are taking part in this trial.

Information which identifies you will not be published or shared.

Your de-identified trial information will be shared with Astra Zeneca to allow them to continue their research into treatments for bronchiectasis.

What if something goes wrong?

If you are concerned about taking part in the trial, you have the right to discuss your concern with a researcher involved in carrying out the trial or a doctor involved in your care.

If you have a complaint about your participation in the trial, please first talk to a researcher involved in the trial. You can also make a formal complaint. You can make a complaint to a senior member of the research team or to the Complaints Officer:

[LOCAL CONTACT DETAILS]

If you think you've come to harm due to taking part in the trial, there are not any automatic arrangements to get financial compensation, but you might have the right to make a claim for compensation. If you wish to make a claim, you should consider getting independent legal advice, although you might have to pay for your legal costs.

Insurance

The University of Dundee are Sponsoring the trial. The University of Dundee holds professional negligence clinical trial insurance which gives legal liability cover and no-fault compensation for accidental injury.

The Scottish Health Boards which are participating as trial sites, are members of the NHS Scotland Clinical Negligence and Other Risks Insurance Scheme (CNORIS) which gives legal liability cover of Scottish Health Boards for this trial. This will cover their liability for carrying out the trial.

NHS Health Trusts in England have membership of an insurance scheme from the NHS Litigation Authority (NLA).

NHS Health Trusts in Wales have membership of an insurance scheme from the Welsh Risk Pool.

NHS Health Trusts in Northern Ireland have membership of an insurance scheme from the Clinical Negligence Fund.

If you apply for health, life, travel or income protection insurance you may be asked questions about your health. These questions might include questions about any medical conditions you have or have had in the past. You might also be asked if you have had any genetic tests or about taking part in this trial. We don't expect that taking part in the trial will adversely affect your ability to buy insurance. Some insurers may use this information to limit the amount of cover, apply exclusions or increase the cost of insurance. Your insurer may take in to account any medical conditions you have, including any which are diagnosed as part of a research trial, when deciding whether to offer insurance to you.

Data Protection Privacy Notice

How will we use information about you?

We'll need to use information from you and from your medical records for this trial.

This information will include your initials, NHS number, name and contact details. Staff will use this information to do the research or to check your records to make sure that the research is being done properly.

People who don't need to know who you are won't be able to access your name or contact details. Your data will have a code number instead.

We'll keep all information about you safe and secure.

Once we've finished the trial, we'll keep some of the data so we can check the results. We'll write our reports in a way that no-one can work out that you took part in the trial.

What are your choices about how your information is used?

- You can stop being part of the trial at any time, without giving a reason, but we'll keep the trial information about you that we have already collected.
- You can request that all personal identifiable data be removed.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?

You can find out more about how we use your information at:

- www.hra.nhs.uk/information-about-patients/
- <https://www.dundee.ac.uk/information-governance/dataprotection/>
- http://www.nhstayside.scot.nhs.uk/YourRights/PROD_298457/index.htm

Contact details for further information

Thank you for taking time to read this information and for considering taking part in this trial.

If you'd like more information or want to ask questions about the trial, please contact the trial team using the contact details below.

Principal Investigator: [TBC]

Researcher Nurse: [TBC]

You can contact us Monday – Friday between 09:00 -17:00.

Outside of those hours, if you need advice, you can contact your out of hours GP service/NHS24 via 111.

