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| PARTICIPANT INFORMATION SHEET |

# AIR-NET: Testing anti-inflammatories for the treatment of bronchiectasis.

# 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. At the moment, there are 3 medications being tested but new medications may be added. initially we expect about 170 participants will take part in the trial but as more test medications are added more participants will be asked to take part.

You may be able to take part in this trial if you have bronchiectasis. The trial doctor will check to see if there are any reasons why the trial would not suit you. You will not be able to take part if you are pregnant, breastfeeding or planning a pregnancy (male or female).

# Why are we doing this trial?

We want to find new treatments that can help improve symptoms and reduce chest infections in people with bronchiectasis. New ways of doing clinical trials, which tested several medications at the same time, were lifesaving during the COVID-19 pandemic. This type of trial gave us dexamethasone which became the first effective treatment for COVID-19. Learning from that experience, we are conducting a trial in bronchiectasis where we test several medications at the same time. This way we hope will find a new, effective treatment more quickly and efficiently.

Symptoms of bronchiectasis are caused by inflammation in the lungs. The purpose of this trial is to look to see if medications with anti-inflammatory properties can be used to treat bronchiectasis. The medications being tested are already used to treat other medical conditions. We have chosen these medications to test because in the laboratory they also have shown anti-inflammatory effects. We hope that the anti-inflammatory properties of the trial medications will work on inflammation in the lungs. We will measure whether these treatments have effects on inflammation in the lungs by measuring a sputum test called neutrophil elastase (NE) and through blood tests. We will want to see if the trial treatments help improve lung inflammation and whether this also improves participant’s quality of life.

Testing medications that are already approved for other health conditions is common in clinical trials, this is called drug re-purposing. Doing trials on already approved medications has many benefits. It gives us the chance to use existing medications in different ways, this could offer future treatments to help improve lives faster. It is hoped that the medications being tested in this trial will reduce lung inflammation and symptoms in bronchiectasis.

This trial is different from a usual clinical trial where one medication is being tested against one control group. In this trial, several medications are being tested at the same time. This offers several benefits: instead of doing lots of different trials, we can find out in one trial whether any of these medications work against lung inflammation. This could offer new treatment options much quicker to people living with bronchiectasis.

The main aims of this trial are to find out:

* if any of these medications reduce lung inflammation in bronchiectasis?
* if these medications can be taken safely by people who have bronchiectasis?
* if any of these medications improve quality of life for people living with bronchiectasis?

# What is being tested?

AIR-NET is a platform trial, which means several medications are being tested at the same time. It also means that that we may add some other test medication options as the trial continues.

This trial will compare the health of people treated with medications with anti-inflammatory properties to people who do not receive any trial medication but continue with their usual bronchiectasis treatment (usual care). Each participant in the trial will receive only one of the trial medications or will receive usual medical care, with no additional trial medication.

The medications we’re using are currently used by the NHS for different reasons. They have been used for a long time and are well tolerated. All these medications have been shown to reduce inflammation in the lungs.

If you agree to take part in the trial, you will be assessed to see if it is ok for you to take all the trial treatments. You will then be allocated by random to one of these treatment options. If any of the trial treatments are not suitable for you, or you don’t want to take any of the medications, you will not be allocated that treatment option. Your treatment option will then be decided at random (like tossing a coin but using a computer).

The four treatment options are:

|  |  |
| --- | --- |
|  | Dose |
| Usual care  Continue with usual bronchiectasis treatment | Not applicable |
| Disulfiram  Used to treat alcoholism and has anti-inflammatory properties | 2 tablets, once a day |
| Dipyridamole  An anti-platelet medication used to prevent blood clots, which has anti-inflammatory properties | 1 capsule, twice a day |
| Doxycycline  An antibiotic with anti-inflammatory properties that is used to treat a range of bacterial infections | 1 capsule, once a day |

Depending on the number of participants allocated to each treatment, we might stop adding more participants to some treatment options. We will tell you what treatments are available to you and what treatment you have been allocated.

If you are allocated to usual care, you will continue your current bronchiectasis treatment as usual. If you are allocated to one of the trial medications, you will be given the trial medication and you will be asked to take this for 28 days. You’ll receive a medication information leaflet about the medication you’re allocated to. Please read this for full instructions of how to take the medication and possible side effects.

# How do I take my trial medication?

Disulfiram: You should take 2 tablets once a day for 28 days. Take your medication at the same time each day with water.

It is important that you do not drink alcohol for 24 hours before starting your first dose of medication, when you are taking the medication and for 14 days after your medication has ended.

Dipyridamole: You should take 1 capsule two times a day for 28 days. Take one capsule in the morning and one capsule in the evening with meals. Take your medication at the same time each day. The capsules should be swallowed whole without chewing.

Doxycycline: You should take 1 capsule once a day for 28 days. The capsules should be swallowed with plenty of water. It is best to take your capsules at the same time each day, when sitting or while standing. It is important not to lie down for at least thirty minutes after taking Doxycycline capsules, so that the capsule can move as swiftly as possible into the stomach and prevent irritation of the throat or oesophagus (canal taking food from the mouth to the stomach). If Doxycycline capsules upset your stomach, then taking it with food or milk is recommended.

If you forget to take a dose of your medication, take it as soon as you can. Take your next dose at the right time. Do not take a double dose to make up for a forgotten dose.

Please contact the trial team if you have any questions or experience any side effects.

Please bring back your medication box once the treatment is complete, with any remaining capsules and also if it is empty.

# 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 this trial and future trials.

# What will happen to me if I take part?

A diagram of a treatment procedure

Description automatically generatedYou will be in the trial for approximately 3 months. This will involve you attending hospital for 6 appointments during that time.

## Visit 1

The first appointment is a screening visit where we’ll carry out assessments to see if the trial is suitable for you. This visit will take around 2 ½ hours. We’ll ask you to complete a consent form to confirm that you wish to take part in the trial. You’ll be able to speak to a trial doctor before you sign the consent form if you want. Your consent will remain in place even if you lose the capacity to give consent. If this happens and further consent is needed, we will ask a personal or professional legal representative to give consent on your behalf.

We’ll give you a physical examination and ask about your medicines and illnesses and check your medical notes. We’ll then carry out some assessments.

Please see in the table below what assessments will be carried out at each visit.

If your sputum sample shows a positive result for inflammation and if you are otherwise suitable for the trial, then you will be invited to join the trial and attend visit 2. If you are found to be not suitable for the trial, you will not be able to take part in the trial and the reasons for this will be explained to you.

## Visit 2

Visit 2 will take place in the next month. This visit will take around 2 hours. You’ll be asked about your health and any changes to your normal medications. You will then be allocated one of the trial treatment options. If you are allocated one of the trial options which includes a trial medication, we will give you enough for the next 28 days. You will start taking trial medication the day after this visit.

## Visits 3 and 4

You’ll come back after 1 week (visit 3) and again after 2 weeks (visit 4), each visit will take around 1 ½ hours. At these visits you’ll be asked about your health and any changes to your normal medications.

## Visits 5

After taking the trial medication or continuing your usual care for 4 weeks, you will come back for another trial appointment, this will last around 1 ½ hours. If you were allocated a trial treatment, you will be asked to bring back your medication bottle to collect any unused medication.

## Visit 6

This is the last visit for the trial and will be 1 month after you have finished the trial treatment.

At each visit you will be asked if there are any changes to your medication or if you have experienced any exacerbations. If you experience an exacerbation, you might be asked to attend for an additional visit to review your symptoms.

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| --- | --- | --- | --- | --- | --- | --- |
| Trial Assessments | Visit 1 | Visit 2 | Visit 3 | Visit 4 | Visit 5 | Visit 6 |
| Consent form | X |  |  |  |  |  |
| Health & medication checks | X | X | X | X | X | X |
| Physical examination | X |  |  |  |  |  |
| Height & weight | X |  |  |  |  |  |
| Blood pressure, pulse, temperature & oxygen level | X | X | X | X | X | X |
| ECG | X |  |  |  |  |  |
| Spirometry | X | X | X | X | X | X |
| Questionnaires | X | X | X | X | X | X |
| Symptom diary (every day from visit 2 – visit 5) |  | X | X | X | X |  |
| Blood samples | X | X | X | X | X | X |
| Sputum sample | X | X | X | X | X | X |
| Nasal sample |  | X |  |  | X |  |
| 6-minute walk test |  | X |  |  | X |  |
| Pregnancy test (if applicable) | X | X | X | X | X |  |
| Treatment allocation |  | X |  |  |  |  |
| Return of unused medication |  |  |  |  | X |  |

Description of assessments:

* Height and weight
* Blood pressure, pulse and 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
* Spirometry – after you have been given a short-acting bronchodilator for example, 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 short-acting bronchodilator inhaler e.g. salbutamol, 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.
* Patient diary – you will be asked to complete a symptom diary every day during your treatment to monitor your bronchiectasis symptoms. You can either complete the symptom diary on paper (which will be provided) or electronically. If you would like to complete the diary electronically, you will have the choice to receive an automatic email every day with a website link to complete the diary, or you can complete the diary on a smartphone application (app). If you choose to complete the diary electronically, you will need to provide your email address to the trial team. Your email address will be accessed by the local research team and the University of Dundee trial team only for the purpose of giving you access to the electronic diary.
* Blood test – we’ll take a maximum of 100ml per visit (up to 7 tablespoons)
* Sputum sample – at visit 1 you’ll be asked to produce a sputum sample that we’ll test foran inflammatory marker (called neutrophil elastase). At all other visits you will be asked to provide a sputum sample for the trial research. 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.
* Nasal swab – a swab of the inside of your nose, which is less deep than a COVID test.
* 6-minute walk test – an exercise test to measure how far you can walk in 6 minutes, you can slow down, stop or rest at any time during the test
* Pregnancy test (urine) for women of childbearing age

# What will my blood, sputum and nose samples be used for?

During the trial blood, sputum and nose 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. Any spare blood leftover after the research lab has carried out these tests will be stored so researchers can use it in the future. Any researchers will have to get ethics committee approval to use your spare blood. This may include use by commercial organisations. Some of the spare blood may be used for genetic analysis to identify inherited factors that influence the development of disease. You can let us know if you do not want this spare blood to be stored for future use.

Sputum samples

* At the screening visit we will check to see if you havean inflammatory marker in your sputum to determine if you are able to take part in the trial.
* Biomarker sputum samples: for the research lab to check markers of lung inflammation.
* As part of this trial, any leftover sputum sample from each visit will be stored so that researchers can use it in the future. Any researchers will have to get ethics committee approval to use your samples. This may include use by commercial organisations. You can let us know if you do not want this spare sputum to be stored for future use.

Nasal samples

* We will look to see if the treatments make any change to inflammation in the lining of the nose or changes to other important parts of the condition like mucus.

# 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.

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

# What will happen when the trial finishes?

The trial medications 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 shows a possible benefit from the medicine being tested it is likely that more trials with larger numbers of participants will be needed.

We will compare the results of the assessments for each treatment with the results from the participants who were allocated to continue their usual care. It will take a few years to complete the trial and publish the results. We will send you a letter with the results once we have them.

If you want you can join the trial again. You will have to sign another consent form and you will be allocated a treatment. Because the treatments are allocated randomly, there is a chance that you might get the same treatment as before. You will be able to do the trial a total of 3 times, if you want. Talk to your research team if you want to do the trial again.

# What are the possible benefits of taking part?

There are currently no licensed or approved treatments for bronchiectasis. The main benefit of taking part will be contributing to the possible development of new treatments which could benefit you and future patients. 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.

The medications being tested have anti-inflammatory properties and we hope that these might reduce your bronchiectasis symptoms or exacerbations.

You will 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 shows any new abnormality which the trial doctor thinks is significant, we’ll tell you. If you agree, we will also tell your GP or refer you to a specialist clinic at the hospital if needed.

# What are the possible disadvantages and risks of taking part?

The medications being tested in this trial have been approved for use for the treatment of other health conditions. However, any medication can have side effects, the known side effects for these medications are listed below. All of the medications being used in this trial have been used safely in the NHS for other conditions and most people take these medications without experiencing serious side effects.

You will receive a trial contact card with the research team contact details. If you experience any symptoms that you think may be due to the trial medication, please contact your trial team to report this.

Disulfiram:

Disulfiram blocks the body’s usual routes to break down alcohol, causing unpleasant side effects after drinking alcohol, and is currently licensed to treat alcohol dependence. Disulfiram also has anti-inflammatory properties.

You cannot drink alcohol while taking this medication. If you are allocated to take this trial medication, you will not be able to drink alcohol for 24 hours before treatment, for the 28 days of treatment and for 14 days after treatment finishes. Drinking alcohol while taking this medication can make you feel unwell giving you a reaction, which may cause flushing, nausea, vomiting, headache, dizziness, heart palpitations, low blood pressure or collapse. If you believe you have accidentally taken alcohol while using this medication, please contact the trial team immediately for advice.

If you do not want to stop drinking alcohol while you are in the trial, let your trial team know. You can still take part in the trial but you will not be allocated disulfiram.

Your liver function will be monitored throughout the trial by collecting a blood sample at each visit because this treatment has been occasionally found to cause liver problems. The medication will be stopped if any liver problems are identified. Other possible side effects include drowsiness, nausea, vomiting, rash, depression or psychosis. Most people who take this medication do not experience these side effects.

Dipyridamole:

Dipyridamole is a blood thinner that is currently licensed to prevent blood clots and strokes. Dipyridamole also has anti-inflammatory properties.

Most people who take dipyridamole do not report side effects. If it does cause side effects the most common are headache, dizziness, diarrhoea, nausea and rash.

Doxycycline:

Doxycycline is an antibiotic with anti-inflammatory properties that is used to treat a range of bacterial infections, including bronchiectasis exacerbations. Most people who take doxycycline do not experience any side effects. If side effects occur, the most common are rash, diarrhoea, vomiting, headache and photosensitivity/sunburn.

If you develop any reaction to the medication 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 the trial.

# **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. This is because the possible fertility effects of these medications are unknown. Therefore, both male and female participants taking part in the trial should avoid becoming pregnant during the trial duration.

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.

If you withdraw from the trial all information and samples collected up to that point will be kept by the research team. All personal identifiable data can be withdrawn, should you request it.

# Will I receive any payment for taking part?

You will receive £100 for each visit you attend to cover travel expenses and compensation for your time. This payment may be cash or a voucher, depending on the local NHS payment policies. If you receive benefits, you may need to check what type of payments you can accept, as this may affect your benefit payments. https://www.nihr.ac.uk/documents/payment-guidance-for-members-of-the-public-considering-involvement-in-research/27372

# 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 LifeArc, a medical research charity. 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?

Patient partners from the European Lung Foundation have been involved in developing the design of the trial and will be involved in the running of this trial. They have also helped to write this information sheet.

Who has reviewed this trial?

This trial has been reviewed by London Central REC committee.

# 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 trial team either on paper or on their local NHS computers. Only certain members of the trial 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 trial 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 trial 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. De-identified trial information may be shared with approved research partners to help bronchiectasis research.

# 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 trial 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 Clinical Trials indemnity cover which covers the University’s legal liability for harm caused to patients/participants

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. 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 or CHI 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.

The Sponsor is responsible for looking after your information. We’ll keep all information about you safe and secure.

We may share data about you outside the UK for research related purposes to:

* Complete the analysis of the trial results
* To continue research into bronchiectasis treatments

If this happens, we will only share the data that is needed. We will also make sure you can’t be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

* our partners who analyse your data
* future researchers who are doing ethically approved research

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

* (some of) the countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK
* we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details [visit the Information Commissioner’s Office (ICO) website](https://ico.org.uk/for-organisations/uk-gdpr-guidance-and-resources/international-transfers/)
* we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
* we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing
* we have procedures in place to deal with any suspected personal data breach.  We will tell you and applicable regulators when there has been a breach of your personal data when we legally have to. For further details about UK breach reporting rules [visit the Information Commissioner's Office (ICO) website](https://ico.org.uk/for-organisations/report-a-breach)

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

We will keep your trial data for the minimum period of time required by the UK regulatory authorities, 25 years. The trial data will then be fully anonymized and securely archived or destroyed.

# 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 have the right to ask us to remove, change or delete data we hold about you for the purposes of the trial. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this
* If you agree to take part in this trial, you will have the option to take part in future research using your data saved from this trial.

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

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

* <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/templates/template-wording-for-generic-information-document/>
* <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 or NHS111 (England and Wales)NHS24 (Scotland) by phoning 111.

Trial website <https://sites.dundee.ac.uk/air-net/>

