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Participant Information Sheet

Seven versus Fourteen Days Antibiotics for Patients with Bronchiectasis Requiring Intravenous Antibiotics- SBIVA Study

You are invited to take part in a research study. To help you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for your time

FUNDED BY
NIHR | National Institute for Health and Care Research

What is the purpose of the study?

Bronchiectasis affects around 300,000 people in the UK. International guidelines recommend that patients receive intravenous antibiotics for 14 days if they are particularly unwell, have an infection with resistant organisms, or if oral antibiotics are ineffective. The duration is based on expert advice but there have not been any studies confirming what length of course is best. There is some evidence to suggest that patients receiving 7 days of intravenous antibiotics took longer to next exacerbation (flare up) compared to those receiving treatment for 14 days. Treating for too long may keep people in hospital longer than needed or increase their risk of antibiotic side effects, whereas treating for too short a period may increase the risk of an infection soon after completion of antibiotic therapy.

We want to investigate whether seven or fourteen days of intravenous antibiotics is best for patients experiencing a flare up of their bronchiectasis.

We will select 400 patients throughout the UK who need intravenous antibiotics. Half, at random, will receive 7 days of intravenous antibiotics and the other half will receive 14 days of intravenous antibiotics. Both groups will get standard care in addition.

We will measure the duration of time (up to one year) between starting intravenous antibiotics until needing another course of oral or intravenous antibiotics for an exacerbation of bronchiectasis (time to exacerbation) in each group to see which is shorter.

Why have I been invited to take part?

You have been asked to take part as you have been diagnosed with bronchiectasis and have already started intravenous antibiotics for an exacerbation of bronchiectasis **or** may need a course of intravenous antibiotics for an exacerbation of bronchiectasis within the study time period.

Do I have to take part?

No, it is up to you to decide whether to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive, or your legal rights.

What will happen if I take part?

Once you have read this leaflet you can have as much time as you need to decide whether to take part in the study prior to experiencing a flare up of your bronchiectasis. If you are interested in taking part, please return the Consent to Researcher Contact Form using the prepaid envelope or call the research team on <Insert Contact Details>. If you have not received the Consent to Researcher Contact Form or a prepaid envelope, please call the research team directly using the contact details provided.

Once we have confirmation from you that you are interested in joining the study **and you are experiencing a flare-up of your bronchiectasis** the research team will arrange a screening /baseline appointment. At the appointment, the researcher will discuss each part of the study with you and answer any questions you have. If you are happy to take part, we will ask you to sign a consent form.

You may be asked if you wish to join the study when you are already receiving urgent care i.e. intravenous antibiotics. Once you have read this information sheet you will have the opportunity to discuss the study with a member of the research team and have any questions answered. You will have up to 3 days from the start of your intravenous antibiotic treatment to decide whether to take part, as all patients must be randomised into the study by the time you start your fourth day of antibiotic treatment. If you are happy to take part you will be asked to sign a consent form.

You will be asked to participate in two research appointments – one to join the study (baseline/screening) and one at day 14 from start of intravenous antibiotics. We will do our best to match these with your clinical appointments or inpatient stay. If you are unable or would prefer not to attend the research site for your day 14 appointment, we can arrange to carry this out remotely by telephone or by using videoconference facilities. The research activities will take around an hour to complete. You will then receive a telephone call once a month for a year. At your appointments you will be asked for the following:

Screening and Baseline visit (visit 1; approximately 1 hour)
Once consent has been provided, eligibility will be confirmed as per the study inclusion and exclusion criteria. The researcher will ask you questions about your health to ensure you are suitable to take part in the study. We will collect information from you which will include your name and address, telephone number, email address (if you have one), date of birth, NHS number (e.g. Community Health Index number (CHI) or hospital number), demographics and medical history.

Pregnancy test (5 minutes): Women of child bearing potential will be required to have a negative pregnancy test as part of the screening procedures, as taking the study drug is not advisable for pregnant women.

Randomisation process: Before randomisation, a lung function assessment (spirometry, lasting approx. 15 minutes) may be required if it is more than one year since your last assessment or if the results of your last assessment are not available.

After eligibility has been confirmed you will be allocated at random (randomised) by a computer to one of two groups. One group will receive intravenous antibiotics for 7 days and the other for 14 days. Participants who are already receiving intravenous antibiotics, (up to a maximum of 3 days) will have the number of days already received deducted from the overall total. For example: a participant who has already had antibiotics for 2 days that is randomised to the 14 day group, will continue to receive antibiotics for a further 12 days, making the total days of antibiotic treatment 14.

Antibiotic Prescription and dosing instructions: The antibiotic that we are using in the study is called Meropenem. This is a broad spectrum antibiotic commonly used in the treatment of bronchiectasis. Participants who have not yet started intravenous antibiotic use will be prescribed 7 or 14 days of Meropenem according to their allocated group. Participants that have already started Meropenem will continue to receive Meropenem for the remainder of their 7 or 14 day allocated period. In certain circumstances, alternative antibiotics may be prescribed. For example: supply issues, patient allergies or if in line with local hospital policy. Permitted alternatives are Piperacillin-tazobactam; Ceftazidime; Ciprofloxacin; Aztreonam; Gentamicin; Colistimethate sodium. Participants who have already started an intravenous antibiotic other than those listed will be changed onto Meropenem or one of the approved alternatives for the remainder of their 7 or 14 day allocated period.

If you receive your antibiotic treatment as an inpatient at hospital, you will receive treatment and care as per usual hospital policy/practice.
If you will self-administer treatment, you will be taught how to do this as per usual hospital practice and discharged with your medication.

Questionnaires: You will be asked to complete the following questionnaires (these will take approximately 15-20 minutes to complete them all):

- St. George's Questionnaire
- Bronchiectasis Health Questionnaire
- CAT Questionnaire
- Euroqol 5 Dimension Health Related Quality of Life Survey (5 level version, EQ-5D-5L)
- Health Care Resource Use (HCRU)

If possible links will be emailed to you so you can complete questionnaires electronically. If you are unable or unwilling to complete the questionnaires electronically, paper copies will be provided to you and collected by the study team for review after completion.

Sputum sample(s): If you are able to cough up any sputum, a sample will be collected and sent to your local NHS microbiology laboratory for routine analysis.

Patient diary (up to Day 14): You will be given a paper diary to complete to record how many doses of your antibiotic you have taken each day, and whether you have done any breathing exercises. The study team will review the diary card with you at the Day 14 assessment (see below).

Line removal (around day 7 or 14)
After completion of antibiotic treatment, participants who have self-administered and completed their course of treatment at home will return to clinic to have line removal as per usual local practice.
Participants who received their treatment as an inpatient will have their line removed prior to hospital discharge as per usual local practice.

Day 14 Assessment (all participants; approximately 30 minutes)
The day 14 assessment may take place in person, over the telephone or by video call. At this assessment, your patient diary will be reviewed and you will be asked to complete the same questionnaires that you did at your baseline visit (described above). If you are able to cough up any sputum, samples will also be collected as above. If this study visit takes place remotely (via telephone or video call), you will be asked to report your sputum colour to the study team using a sputum colour card provided to you and send your sample back to the hospital, in a secure postal box. You will be provided with separate instructions about how to do this from your local research team.

Monthly Telephone Call (10-15 minutes, for 1 year)
After you have completed your treatment, a member of your research team will phone you once a month for a year to see how you are doing and to complete the EQ5D5L and HCRU questionnaires with you. The call will take approximately 10-15 minutes. The last monthly call will take place 12 months after you started your study intravenous antibiotics and this will be your last contact with the study team.

Future Treatment
Once you have completed your 7 or 14 day course of study intravenous antibiotics you should return to your usual care team (GP or clinic) if you feel unwell with a flare up of symptoms.

Identification of First Exacerbations (Flare-Up)
One of the most important aspects of this study is to identify when your first exacerbation of bronchiectasis (flare up) occurs after completing your course of intravenous study antibiotics.
It is therefore very important that you call the local study team within 7 days of starting any antibiotics for your bronchiectasis. The local study team will review your symptoms with you to see if they meet the definition of first exacerbation by the agreed study criteria.

If you are able to cough up any sputum we will ask you to send a sample back to your local site (using secure postal boxes) when you are starting antibiotics for the first time after your course of study intravenous antibiotics. You will be provided with separate instructions about how to do this from your local research team.

If the physician or research nurse deems this is not an exacerbation by the agreed criteria, then you will continue until you feel you have the next exacerbation and again will then be checked by the physician / research nurse. This will continue until you meet the agreed exacerbation criteria.

We will ask you to send a sputum sample back to your local site if you are starting antibiotics again if the first time you did this it was not verified.

Identification of Flare-Ups after the first exacerbation is verified
Any further flare ups will be recorded during monthly telephone calls but do not need verified by the physician / research nurse so there is no need to call us within 7 days of starting antibiotics after that first exacerbation is verified.

Your involvement at a glance

Visit Name	Where will I be ?	What will happen ?
Baseline/screening	At hospital appointment with study team	Spirometry (if required) Pregnancy test (if required) Sputum sample (s) Medical history Questions about medications you are taking Randomisation Questionnaires (x5)
Treatment	In hospital or at home	Administration of intravenous antibiotics for 7 or 14 days Diary card for 7 or 14 days
Line removal	At hospital clinic or ward	Line removal
Day 14	At hospital clinic visit or at home	Sputum sample (s) Sputum colour Questions about medications you are taking, and your symptoms Review of diary card (s) Questionnaires (x5)
Time of First Exacerbation	At home	Questions about medications you are taking and your symptoms Sputum sample (s)
Monthly Telephone call up to one year	At home	Questions about medications you are taking and your symptoms Questionnaires (x2)

Optional SBIVA Sputum Microbiome sub-study (participating centres only)
In addition to the main SBIVA study, you are invited to take part in the optional SBIVA Sputum Microbiome Sub-study. If you agree, you will be asked to provide (if you are able) an additional sputum sample at Baseline/screening, day 14 and at the time of your first exacerbation after completing the study antibiotics.

The aim of the sub-study is to investigate characteristics of the microorganisms (e.g. different types of bacteria) involved in bronchiectasis exacerbations, and how their environment (microbiome) is associated with treatment and clinical outcome. Sputum samples collected during the trial will be sent to the Wellcome Sanger Institute where they will undergo specialised analysis. The results of the analysis will be deposited in the European Nucleotide archive (ENA)). Non-identifiable information will be sent to the Wellcome Sanger Institute which will include: unique patient ID, site name, the date and time of sample collection and clinical outcome.

The analysis from this sub-study will be presented in published manuscripts in academic journals. All data will be published in a way that will not identify participants.

Any leftover sputum may be sent to an external commercial service for metabolomics analysis. No data will be shared with the external service.

Is there anything I need to do or avoid?

There are no special things you need to do or avoid when taking part in this study.

If you need to do a Spirometry Lung Test before you are randomised, you will need to do the following to prepare:

Avoid eating a large meal for 2 hours before the test
Avoid caffeine on the day of your test
Avoid vigorous exercise for 30 minutes before the test
If you use an inhaler, make sure you have taken this at least 60minutes before the test
Bring your inhalers (plus any spacer device) to the appointment
Wear loose fitting comfortable clothing

What are the possible benefits of taking part?

One of the reasons for running this study is to establish any benefits for patients receiving a shorter course of antibiotics and participation in this study may help to improve bronchiectasis health care in the future.

We have shown in a smaller study that patients who received a shorter duration of antibiotics took longer until their next flare up of their bronchiectasis. Reduction of antibiotics leads to less hospital acquired infections and healthcare resource use.

We anticipate that if you are assigned to the 7 day treatment arm it may delay the time to next needing an antibiotic for a flare up. Your treatment will be less burdensome as only 7 days as opposed to 14 days treatment is needed. Receiving a shorter duration of antibiotic treatment than the standard course may reduce the risk of developing antibiotic resistance and experiencing fewer or shorter lived side effects.

The benefits to you taking part in this study if you are allocated to the 14 day treatment arm are the same as if you received standard care.

What are the possible disadvantages of taking part?

The antibiotic medicines used in this study, are commonly used for respiratory infections and have known possible side effects. The known possible side effects from the drugs we are using in the study include the following; diarrhoea, nausea, vomiting, constipation, dyspepsia, abdominal pain, infection, insomnia, headache, dizziness, rash, pruritus (itching), fever, injection/infusion site reactions, and the alteration of some blood cell counts and blood tests relating to liver and kidney function, blood clotting and anaemia. The possible side effects are the same as if you were not in the trial and were receiving 14 days of intravenous antibiotics for a flare up of your bronchiectasis.

There are not thought to be many disadvantages to taking part in the study. It does involve you taking time to provide sputum samples, complete the patient diary for 7 or 14 days, complete questionnaires and take part in monthly telephone calls for a year.

Some of the questions in the questionnaire are of a sensitive nature. If completing the questionnaires have caused you to feel in any way upset and you feel you need help and support, then please see below for a list of people to contact:

- Make an appointment to see your GP to discuss your concerns.
- There are many helplines you can call if you are feeling down or want to talk.
  - Asthma+Lung UK offer support for people living with a lung condition. They can be contacted by telephone on 0300 222 5800 or emailed helpline@asthmaandlung.org. Further information is available on their website www.asthmaandlung.org.uk
  - The Samaritans offer support for anyone needing someone to listen. You can call them on 116 123. More information on other support agencies can be found on the NHS website, www.nhs.uk

What if there are any problems?

If you have a concern about any aspect of this study please contact <insert name and contact details here> who will do their best to answer your questions.

If any new information become available during the study that you need to be aware of, we would write to you to let you know.

In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against NHS **[XXXX]** but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

What will happen if I don't want to carry on with the study?

If you no longer want to take part, you are free to stop at any time and this will not affect the healthcare that you receive, or your legal rights. You should speak to the research team to let them know you no longer want to take part and they will discuss with you whether you want to:

(i) Stop taking your medication but you are happy to continue with study follow up (study diary, sputum sample(s), questionnaires, telephone calls).

(ii) Stop taking medication, and stop study follow up (diary, sputum sample(s), questionnaires, telephone calls) but you are happy for us to continue to collect information about you from routine medical records.

(iii) Stop taking medication, stop study follow up and stop any new information being collected about you.

Please note that for all options data collected up to the point of withdrawal will be retained by the trial and included in the study results.

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.

What happens when the study is finished?

After the study is finished your identifiable data will be stored for 5 years. After this period they will be disposed of securely unless you have given us permission to retain for future research.

If you have given us permission to store your identifiable data, we might do further research about how good your health is over a number of years. We can do this research by reviewing your medical records and would not need to contact you again. This is optional and we would ask an Ethics Committee for permission before we do any new research using your information.

Your sputum samples from the main SBIVA study will not be kept after the sputum tests have been done. The results from the test will be stored with your clinical notes on an NHS database with a high level of data protection.

If you have consented to the SBIVA Microbiome sub-study and have given us permission to store any leftover sputum samples, we may use them for future ethically approved research studies.

At the end of the study we will make the study data available for other researchers to look at. Before we make it available we will make sure it does not contain any of your personal data. Any study using your anonymised data will require review by a Research Ethics Committee. We will retain anonymised study data indefinitely.

Will my taking part be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage.

How will we use information about you?

We will need to use information from you, from your medical records and the results of your sputum samples for this research project.

We will collect your Community Health Index (CHI) number or National Health Service (NHS) number. Note that the CHI is a population register, used in Scotland for health care purposes. The CHI number uniquely identifies a person on the index and is personal identifiable information. Your CHI number or NHS number is being collected to allow us to check microbiology results.

Other personal identifiable information collected will include your

- Initials
- Name
- date of birth
- ethnicity
- address
- post code
- telephone number
- e-mail address

People 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 do not need to know who you are will not be able to see your name or contact details. Your data will have a code number assigned instead.

We will keep all information about you safe and secure in [NHS Site] and the University of Edinburgh.

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

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from [central NHS records/ your hospital]. If you do not want this to happen, tell us and we will stop.

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/
- our leaflet available from **www.hra.nhs.uk/patientdataandresearch**
- by asking one of the research team
- by sending an email to dpo@ed.ac.uk (University of Edinburgh Data Protection Officer).

What will happen to the results of the study?

This study will be written up and submitted for publication in a medical journal. It is likely that the results will also be presented at academic meetings or conferences. Once the study has been published a summary of the findings will be available on the Edinburgh Clinical Trials website (https://www.ed.ac.uk/usher/edinburgh-clinical-trials/our-studies/all-current-studies/sbiva)

Asthma + Lung UK have agreed to help circulate the results. You will not be identifiable from any published results.

Who is organising and funding the research?

This study has been organised by Professor Adam Hill (Consultant Respiratory Physician at the Royal Infirmary of Edinburgh) and Edinburgh Clinical Trials Unit. It is sponsored by The University of Edinburgh and NHS Lothian (ACCORD), and is being funded by the National Institute for Health Research Health Technology Assessment Programme (NIHR HTA) (Ref: NIHR 133876).

Who has reviewed the study?

The study proposal has been reviewed by the NIHR HTA programme, Asthma + Lung UK and the patient group “Breathtakers, Action for Bronchiectasis”.

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. A favourable ethical opinion has been obtained from **Scotland A REC.** NHS Management Approval has also been given.

Researcher Contact Details

If you have any further questions about the study please contact <insert name> on <insert phone number> or email on: **<insert email address>**.

Independent Contact Details

If you would like to discuss this study with someone independent of the study please contact Anna.Lithgow@nhslothian.scot.nhs.uk

Complaints

If you wish to make a complaint about the study please contact:

<insert contact details> to be adapted depending on research site.

Find below the example for NHS Lothian

Patient Experience Team
2 – 4 Waterloo Place, Edinburgh, EH1 3EG
feedback@nhslothian.scot.nhs.uk
0131 536 3370

..Insert site logo>>

Participant ID: **Centre ID (if applicable)**

Participant Information Sheet
Seven versus Fourteen Days Antibiotics for Patients with Bronchiectasis Requiring Intravenous Antibiotics- SBIVA Study

CONSENT FORM

	Please initial
I confirm that I have read and understand the information sheet (V2.0 23/NOV/2023) for the above study.	☐
I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care and/or legal rights being affected.	☐
I give permission for the research team to access my medical records for the purposes of this research study.	☐
I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh and/or NHS Lothian), from regulatory authorities or from the NHS organisation where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data and/or medical records.	☐
I give permission for my personal information (including initials, name, CHI/NHS number, date of birth, ethnicity, address, postcode, telephone number, email address) to be retained on NHS servers and passed to the Edinburgh Clinical Trials Unit at the University of Edinburgh for administration of the study.	☐
I agree (if I am able) to provide sputum samples for the study for routine NHS laboratory analysis.	☐
I give permission for my General Practitioner to be informed of my participation in the study.	☐
I understand that data collected about me during the study will be converted to anonymised data, stored indefinitely for use in future ethically approved studies.	☐
I give permission for my identifiable data to be kept for use in future studies.	Yes ☐ No ☐
I give permission to be contacted by post/email/telephone for trial reminders and updates.	☐
I agree to take part in the SBIVA study.	☐

Participant ID: **Centre ID (if applicable)**

SBIVA Microbiome Sub-Study Consent

I agree to provide sputum samples (if I am able) for the microbiome sub-study. I understand that my anonymised data as described in the PIS will be sent to the Wellcome Sanger Institute as part of this sub-study and to an external commercial service.	Yes ☐ No ☐
I agree to any leftover anonymised sputum sample from the sub-study being used for future ethically approved studies.	Yes ☐ No ☐

Name of Person Giving Consent	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record

..Insert site logo>>

Participant ID: **Centre ID (if applicable)**

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PARTICIPANT CONSENT FORM

If consent was taken verbally this section must also be completed

Reason for using verbal consent:

_____

I, _____(print witness name) confirm that I / a member of the research team_____ (print name of researcher) have read and explained the content of the PIS (Version 2 23/NOV/2023) and confirm that _____ (name of participant) has had any questions answered. I confirm that to the best of my knowledge they understand this information and is willing to participate in (*delete as applicable)*

(1) the SBIVA study only

(2) the SBIVA study and the sub-study

_____
Name of person giving verbal consent

_____ _____ _____
Name of person receiving consent Signature Date

_____ _____ _____
Name of person witnessing consent Signature Date