Study Title: The use of Benralizumab, an interleukin-5 receptor-α monoclonal antibody as treatment of acute exacerbations of airways disease

Acute exacerbations treated with **B**en**RA**lizumab (The ABRA study)

Chief Investigator	**Professor Mona Bafadhel**
Sponsor	**University of Oxford**
Funder	**Unrestricted research grant (AstraZeneca)**

Study Invitation:

We would like to invite you to take part in a research study.

Before you decide to take part, we would like to inform you why the research is being done and how it would involve you.

Please take time to read the following information leaflet and discuss it with others if you wish.

If there is anything that is not clear or if you would like more information please ask us. Our details can be found on the last page.

Why have you been invited?

You have been invited to take part in the study because you have asthma and/or COPD (chronic obstructive pulmonary disease). Having asthma and/or COPD means that sometimes you may get worse with increased symptoms of breathlessness, cough, wheeze, chest tightness, sputum production or sputum discolouration. At the time of an exacerbation you may need to see the doctor or a specialist for additional medication. These episodes are called exacerbations. The main treatment for these exacerbations is a short course of steroids and/or antibiotics. Sometimes these treatments are helpful, but sometimes they do not work well. Importantly, the use of steroids can complicate heart disease, osteoporosis and especially diabetes.

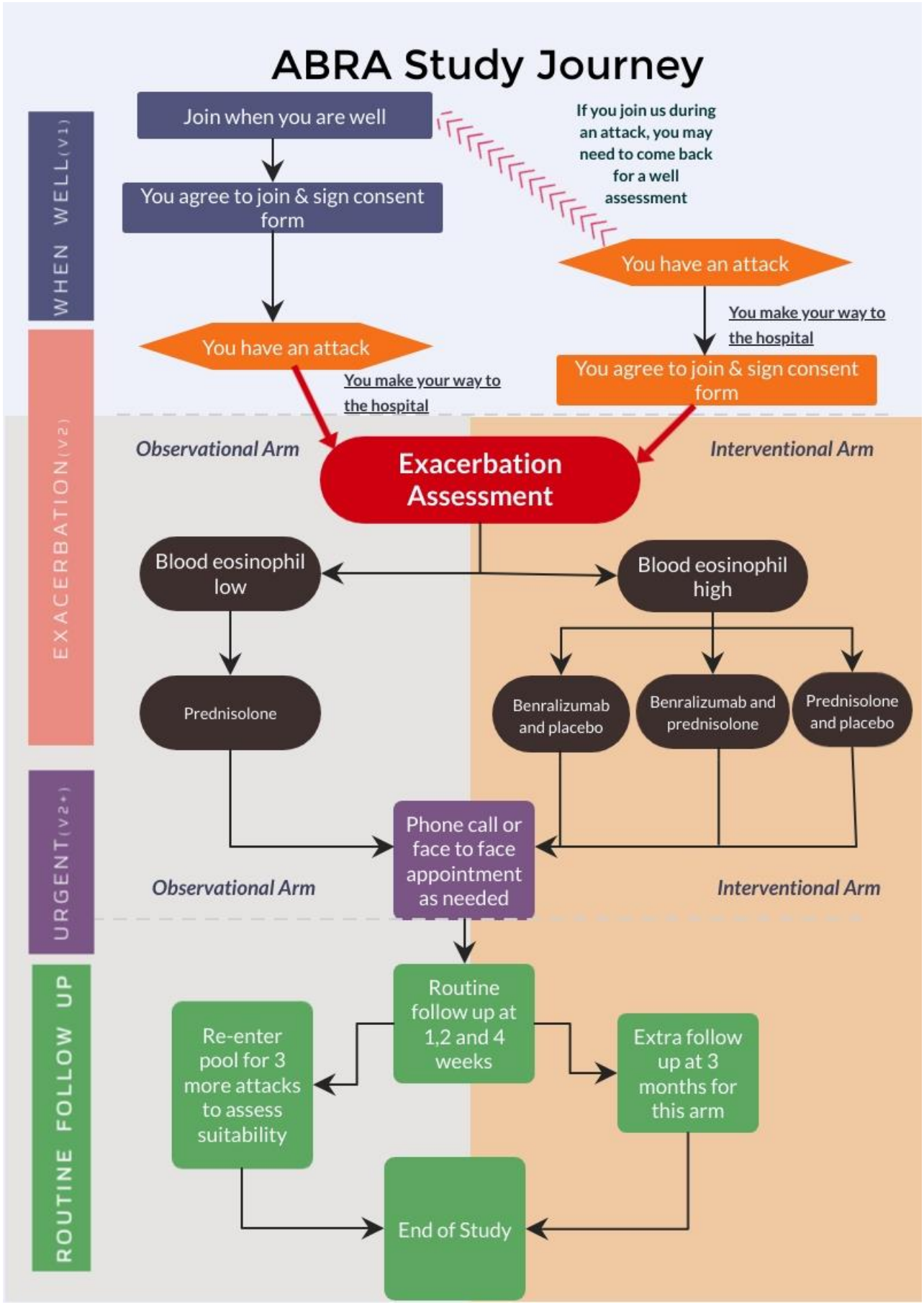
Why are we doing the study?

Some patients with asthma and/or COPD have higher levels of a particular immune white blood cell called the eosinophil. We now know that the presence of raised levels of eosinophils suggests that patients will have a better response to steroid-like medication, such as inhaled steroids, steroid tablets or even specialist injections, which act for a longer time, such as recently approved medicines called Mepolizumab or Benralizumab (from the antibody family of medicines). We also know that lowering levels of eosinophils, by steroid-like medicines, is a main factor in relieving the symptoms of an exacerbation, preventing future exacerbations and treating daily symptoms. However, in certain situations, such as at the time of an exacerbation, steroid tablets, which are often given as part of usual care, do not reduce the eosinophil levels sufficiently, quickly or for long enough. Therefore, patients often report a need to have more steroids, or feel worse and develop more signs of an exacerbation once the steroids are stopped. Repeated courses of steroids are a cause of side effects including thin skin, easy bruising, acid reflux, bone thinning and a higher risk of fractures and diabetes.

We are doing this study in patients with asthma and/or COPD, to test if Benralizumab (given as an injection under the skin) at the time of an exacerbation, alone or in combination with steroid tablets is a better medicine for management of exacerbations in patients with elevated eosinophil counts. We will also study if steroid treatment at the time of an exacerbation in patients with asthma and/or COPD is useful in patients without an elevated eosinophil count.

What is the medicines we are testing?

Benralizumab, the study drug we are testing, is a type of antibody. Antibodies are proteins naturally produced in the body to protect from infection, or foreign substances. Benralizumab acts specifically on the receptor of the eosinophil to reduce eosinophil levels dramatically. Benralizumab is given as an injection under the skin, usually in the arm, upper leg or abdomen; the effect of one injection of Benralizumab acts to reduce eosinophils for 12 weeks. This drug, and similar ones like it, have now been licenced for use in asthma at stable state to decrease asthma attacks. Benralizumab has been studied in acute asthma attacks and has been shown to delay the time to next asthma attack. Benralizumab, and similar ones like it, have also been tested in COPD at stable state. These medicines have proven to be successful, to be safe and to reduce the number of COPD attacks in patients with COPD and high eosinophil levels. **Prednisolone (steroid tablets)** will also be used in this study. This is a standard medicine used for exacerbations of asthma and COPD. Prednisolone is an anti-inflammatory medicine, acting to reduce many cells in the body, including the eosinophils.


ABRA Study Journey
WHEN WELL (V1)
Join when you are well
You agree to join & sign consent form
If you join us during an attack, you may need to come back for a well assessment
You have an attack
You make your way to the hospital
EXACERBATION (V2)
You have an attack
You make your way to the hospital
You agree to join & sign consent form
Observational Arm
Exacerbation Assessment
Interventional Arm
Blood eosinophil low
Blood eosinophil high
Prednisolone
Benralizumab and placebo
Benralizumab and prednisolone
Prednisolone and placebo
URGENT (V2+)
Phone call or face to face appointment as needed
Observational Arm
Interventional Arm
ROUTINE FOLLOW UP
Routine follow up at 1,2 and 4 weeks
Re-enter pool for 3 more attacks to assess suitability
Extra follow up at 3 months for this arm
End of Study

Why do we think you are suitable?

You have been invited to take part in the study because you have asthma and/or COPD (chronic obstructive pulmonary disease) and you have had an asthma and/or COPD exacerbation in the past. We would like to test the study injection in at least 158 patients with asthma and/or COPD having a exacerbation.

Do you have to take part?

The study is voluntary. If you decline or withdraw, this will not affect your care now or in the future. Please contact the study team and ask any questions that you have to help you decide. If you receive this information sheet and are interested in taking part, then please return the reply slip or use the contact details at the end of this information sheet to let the team know you are interested. We will then contact you by telephone or email to discuss the study further.

What will happen if you take part?

This depends on how you join the study (**see page 3).** If you joined us when we invited you at the clinic or you have replied to us via the reply slip or email, we will invite you to the hospital to assess you for the study. If you are suitable and agree to the study, we will obtain written consent from you. This will be called **visit 1**. At this visit, we will check your medical records; ask you questions and perform blood and breathing tests. If your symptoms get worse, with increased symptoms of breathlessness, cough, wheeze, chest tightness, sputum production or sputum discoloration, you may be having an exacerbation. We would like to see you at the beginning of this exacerbation, before you have taken any medication. This exacerbation visit is **visit 2.** We will be able to see you directly at the hospital, where we will perform some breathing and blood tests to see if you are suitable to enter the **'Observational'** or **'Interventional'** study arm. We will then schedule study visits depending on which study arm you are in. We will also use text message or phone call reminders to help you remember to attend all study visits. You can enter directly at visit 2 or after visit 1.

The study arms, study assessments, and study schedule are described below. Women of child-bearing potential will have a pregnancy test at every visit; if you are found to be pregnant you will not be able to enter the study.

What happens if you are in the 'Observational Arm'?

If the eosinophil blood test shows that you do not have a raised eosinophil count then you will be allocated to the '**Observational Arm'**. In this arm, you will receive prednisolone tablets at a dose of 30mg to be taken once a day for 5 days. After this, we would like you to attend follow-up visits at the hospital at 7, 14 and 28 days after the medicines have been given. We will also undertake a medical-notes review after the first time we see you with an exacerbation in this group. If you don't feel better, you can also contact us and we may arrange to see you. This is referred to as unscheduled follow up.

We know that if you have one exacerbation you are more likely to have another one in a 12-month period. If you have been allocated to the **'Observational Arm'**, approximately, 1 in 4 further exacerbations will have a high eosinophil level. If you have another exacerbation in the future, we would like you to contact the study team so that we can test your eosinophils again. **IF** these become elevated, and you have not had prednisolone in the last 30 days, you will be assessed for suitability to enter the

'Interventional Arm'. This is described below. **IF,** however the eosinophils are still low, then we will treat you with standard care (prednisolone tablets and antibiotics if needed), but you would not be required for further visits. We will ask you to contact us again if you develop any further exacerbation symptoms.

What happens if you are in the 'Interventional Arm'?

If the eosinophils are above a certain number, you will enter the **'Interventional Arm'**. In this arm you will be randomly allocated to one of three groups as follows:

- **Group 1** will receive Benralizumab study drug as a single injection (100mg) and one placebo (inactive medicine) tablet taken once a day to take for 5 days.
- **Group 2** will receive Benralizumab study drug as a single injection (100mg) and 30mg of prednisolone tablets taken once a day to take for 5 days.
- **Group 3** will receive placebo injection (inactive medicine) as a single injection and 30mg of prednisolone tablets taken once a day to take for 5 days.

The selection of whether you are in-group 1, 2, or 3 will be chosen by chance and you and the research team will not know what group you have been allocated to. After this, you will attend follow-up visits at 7, 14, 28 and 90 days after the medicines have been given. You can only be given study medicines in the Interventional arm once.

Study visit details

Details of what will happen at these visits is described in this section and as per the study journey diagram.

Visit 1 – Well assessment: This visit will be performed to capture details when you are stable. This visit will be performed at the hospital and is anticipated to last no longer than 2 hours. The study team will:

1. Ask you some questions about your general health and about your asthma and/or COPD.
2. Perform a physical examination and request a chest x-ray if you have not had one in the last 12 months
3. Record your oxygen levels, temperature and blood pressure
4. Record your heart tracing, using an Electrocardiogram (ECG) machine
5. Ask you to fill out some questionnaires about your health
6. Ask you to perform up to 3 types of breathing tests (spirometry, exhaled nitric oxide and impulse oscillometry)
7. Ask to collect no more than 65mLs (5 tablespoons equivalent) of blood
8. Ask to collect a sputum sample, either spontaneously produced or via sputum induction
9. Test your urine for levels of protein, infection, sugar and if you are a woman of child bearing age test your urine for signs of pregnancy.

Visit 2 – Exacerbation visit (Day 0): We would like to see you at the start of an exacerbation or when your symptoms are getting worse. You will be seen by the study doctors to confirm that you are having an exacerbation. You will have study assessments and

a blood test to measure the eosinophil count which will guide us in assigning you to either the **'Observational Arm'** or the **'Interventional Arm'**. This visit is anticipated to take no longer than 2 hours, the study team will:

1. Ask you some questions about your symptoms following your exacerbation
2. Ask you to fill out some questionnaires about your health
3. Perform a physical examination and request a chest x-ray if it is clinically needed
4. Record your oxygen levels, blood pressure and temperature
5. Record your heart tracing using an ECG machine
6. Ask you to perform up to 3 types of breathing test (spirometry, exhaled nitric oxide and impulse oscillometry)
7. Ask to collect no more than 65mLs (5 tablespoons equivalent) of blood.
8. Ask you to complete an electronic diary card of your symptoms relating to breathlessness, cough, wheeze, sputum colour and volume for at least the next 28 days. We will instruct you how to do this.
9. Ask to collect a sputum sample, either spontaneously produced or via sputum induction
10. Test your urine for levels of protein, infection, sugar and if you are a woman of child bearing age test your urine for signs of pregnancy.
11. Make an appointment to see you in 7, 14 and 28 days and if you are in the **'Interventional Arm'** also at 90 days.
12. Dispense the study medication if you are in the interventional arm and prednisolone tablets if you are in the observational arm. We will talk you through how to take the medications and what common side effects to expect (in addition to providing detailed instructions with all medication dispensed).
13. If you receive the study medicine injection you will be monitored following the injection for 2 hours for any signs of drug reaction.

All your usual medication will be continued.

Visit 2+ - Unscheduled follow-up visit (Day 1-3): A telephone follow up visit, or additional study visit may be carried out, if we notice that your symptoms are not improving in the first 3 days following the exacerbation visit. We will be able to check your symptoms on the electronic diary via the tablet. An example of this is shown at the end of this document.

Depending on the improvement in your symptoms, this visit may include:

1. Asking you some questions about your symptoms
2. Performing a physical examination and request a chest x-ray if it is clinically needed
3. Recording your heart tracing
4. Recording your oxygen levels, blood pressure and temperature
5. Ask you to perform up to 3 types of breathing test (spirometry, exhaled nitric oxide and impulse oscillometry)
6. Asking to collect no more than 10mLs (1 tablespoon equivalent) of blood.
7. Testing your urine for levels of protein, infection, sugar and if you are a woman of child bearing age test your urine for signs of pregnancy.
8. Asking to collect a sputum sample, either spontaneously produced or via sputum induction

If we think you need further medical treatment, we will start this directly. This may be more medical tests or additional medical treatment. If another doctor (not a member of the study team) feels that further medical treatment is warranted they will be able to start this and can contact the study team for further information if this is needed.

It is possible that the study medicine will not make you feel better. If this is the case, please contact us and we will arrange to see you. If you are unable to reach us, please contact your GP for a medical assessment. You can also take your own 'rescue pack' medications at any time after you receive the study medicine if you feel that you need it. We will provide you with a prescription for rescue packs if you don't have one. IN AN EMERGENCY, CALL 999. If your symptoms worsen significantly and need to contact the emergency services, please take your study contact card with you. Please let us know as early as you can if any of the above has occurred.

Visit 3-6 - Scheduled Follow up (Day 7, 14, 28, 90*): These follow-up visits will be to determine how your symptoms have been following your exacerbation and the administration of study treatment. These visits will take no more than 90 minutes. The study team will:

1. Ask you some questions about how your symptoms have been since your exacerbation.
2. Record your oxygen levels, blood pressure and temperature
3. Record your heart tracing (day 28 only)
4. Ask you to perform 3 types of breathing tests (spirometry, exhaled nitric oxide and impulse oscillometry)
5. Ask to collect no more than 65mLs (5 tablespoons equivalent) of blood.
6. Ask to collect a sputum sample, either spontaneously produced or via sputum induction
7. Test your urine for levels of protein, infection, sugar and if you are a woman of childbearing age test your urine for signs of pregnancy.
8. Review your medical notes about your symptoms, medication and any consultations that you may have had with the doctor, nurse or any other members of the healthcare team you may have contacted.

End of Study: At the end of your involvement in the study, will be a review of your medical notes. You do not need to attend this visit.

What are the possible side effects, risks and disadvantages of taking part?

If you have a known allergy to prednisolone or Benralizumab, you will not be eligible to enter the study. If your asthma and/or COPD worsens, you will be treated in the manner that you and the study team feel best. If you cannot contact the study team, please seek medical assistance from your nearest doctor or hospital. The study medication may cause some side effects. You may experience none, some or all of those listed here.

Prednisolone side effects: Common side effects of prednisolone (occurring in greater than or equal to 1%) include irritability, depressed mood, euphoria, anxiety, sleep disturbance, confusion, suicidal thoughts, hallucinations and aggression.

Benralizumab side effects: With a new study drug, such as Benralizumab, there may be risks in taking this medication not identified before in earlier studies. We will encourage you to let us know about anything that is troubling you. The study team will follow you closely for the study period. If you experience any side effects described below or new ones, please contact the study team as soon as you can, we will assess and treat you promptly.

- Benralizumab reduces eosinophils. Eosinophils are believed to help fight infections caused by parasites such as tapeworm. Therefore, if you have an infection that is untreated, Benralizumab may reduce your ability to fight parasite/worm infections.
- Similar to other protein-based drugs and other medications, some people may suffer an allergy. These reactions can happen hours or days after the injection. Symptoms may include swelling of the lips, breathing problems, fainting, dizziness, hives/wheals or a rash. Allergic reactions can potentially be life threatening. Please inform the study team or a medical doctor immediately if you think you are having an allergic reaction.
- Other potential allergy like side effects could include:
    - Injection site local reaction, which include itching, redness, pain and swelling
    - Other allergic-type side effects, which include fever, sore throat or headache
    - Development of anti-drug antibodies is a type of allergic reaction, which means the drug may work less well or be associated with allergic reactions that may be life threatening. Once study injection is given, you will be monitored for at least 1 hour and urgent medical treatment if necessary, can be given

To date, Benralizumab has been given in more than 5000 patients with asthma and/or COPD. Many of these side effects listed below also occurred in the patients that received placebo (inactive medicine) and some were more common in patients that received placebo.

- Common side effects occurring more than 3% of the patients included in the studies were
    - Common cold
    - Upper respiratory tract infection
    - Headache
    - Flu
    - Fever
    - Muscle spasm
    - Muscle pain
    - Nasal congestion
    - Back pain
    - Blood pressure (high or low)
    - Worsening asthma and/or COPD

Placebo side effects: Placebo (injection or tablet) does not include an active substance, but contains other substances that can cause an allergic reaction. These symptoms can be very similar to the symptoms listed above.

Study procedure risks: The breathing tests may cause cough, chest tightness and occasional wheezing. Your usual reliever inhaler medicine can be used to relieve these symptoms. The blood samples may cause some mild discomfort but this is expected to cease very quickly.

What are the possible benefits of taking part?

You will receive no direct benefit from being involved in this study. However, we will see you at the time of an exacerbation, assess you fully and treat you. The information we get from this study may be used to improve the treatment of people with asthma and/or COPD in the future.

In case of pregnancy

If you are a woman of childbearing potential, we will request that you use contraception, for 16 weeks after the administration of any study injection and to inform the study team if you become pregnant. If you are a man who is sexually active with partners of childbearing potential, we will request that you use adequate forms of contraception for 16 weeks after the administration of any study injections and to inform the study team if your partner becomes pregnant. If at any time during the study you suspect that you or your partner may be pregnant, please inform the study doctor immediately. If a pregnancy is confirmed, the study doctor will ask for information about the pregnancy. To ensure that any risks to the unborn child are detected as early as possible, the study team will ask to review any relevant medical records and the outcome of all pregnancies will be followed up and documented even if you have discontinued from the study.

Will my general practitioner/family doctor (GP) be informed of my participation?

Yes, if you wish to take part in this study, your GP will be informed.

Will I receive any payment to take part?

Reasonable travel expenses for any visits additional to normal care will be reimbursed on production of receipts, or a mileage allowance provided as appropriate.

Will my information be kept confidential?

All the information you provide (study data) will be kept confidential and secured. If you decide to take part, you will be allocated a unique study number and only specified research personnel will have access to the code to identify your details. Responsible members of the University of Oxford the Oxford University Hospital NHS Foundation Trust may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations. The results of the study may be published in the medical literature but you will not be identified. If there is new information about the study, we will keep you informed throughout and you will always have an opportunity to ask questions throughout the research study.

What happens to any samples I provide?

With your permission, blood and sputum samples that you provide for the study will be used for analysis to measure inflammation. Samples taken at each visit will be processed and collected into de-identified tubes. These tubes will be transported to the John Radcliffe Hospital, without your personal details, and analysed. With your consent, any samples remaining after the analysis for this study will be stored indefinitely to be used for future research studies. Your samples will be used mainly by local researchers, but ethically approved research projects may take place in hospitals, universities, non-profit institutions or commercial laboratories worldwide. These samples will be kept pseudonymised which means that they will contain the study codes that enable your immediate research team to identify them but they will be anonymous to anyone else (no one else will be able to identify you by the study code). If the samples are shared with any other research groups/researchers, they will be fully anonymised to them.

What will happen to my data?

We will be using information from you and your medical records in order to undertake this study. Research is a task that we perform in the public interest. The University of Oxford, as sponsor, is the data controller. This means that we, as University of Oxford researchers, are responsible for looking after your information and using it properly. We will use the minimum personally identifiable information possible. We will keep identifiable information about you for 10 years after the study has finished. This excludes any research documents with personal information, such as consent forms, which will be held securely at the University of Oxford for 10 years after the end of the study. If you agree to your samples being used in future research, your consent form will be held until the samples have been depleted or destroyed. If you agree to your details being held to be contacted regarding future research, we will retain a copy of your consent form until such time as your details are removed from our database but will keep the consent form and your details separate.

The study team will use your name, NHS number, name, address and contact details to contact you during this study and also about future research and informing you of the outcome of this research if you have consented for us to do so. They will keep identifiable information about you from this study for as per local Trust policy for medical notes retention.

Your rights to access, change, or move your personal information may be limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting Professor Mona Bafadhel or Dr Sanjay Ramakrishnan at the following email address abra@ndm.ox.ac.uk

What happens if you want to stop taking part in the study?

You are free to stop taking part in the study at any time without giving a reason. This will not affect the medical care you receive now or in the future. If you would like to withdraw from the study, we will use the data collected up to your withdrawal. Please contact the research team to inform us of your choice.

What happens if there is a problem or if something goes wrong?

If we find anything unexpected, we will let you and your GP know to clinically verify and manage if required. If you have a concern about any aspect of this study, you should ask to speak with the research team who will do their best to answer your questions. Their contact details are given at the end of the document. If you remain unhappy and wish to complain formally, you can do this by contacting the research team or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 616480 or the head of CTRG on email at ctrg@admin.ox.ac.uk. The University of Oxford has arrangements in place in the unlikely event that harm arises to you from taking part in this research study. NHS indemnity operates in respect of the clinical treatment, which is provided.

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study.

If you wish to contact the PALS team please call 01865 221473 or contact via e-mail via PALS@ouh.nhs.uk.

Who is organising and funding the research study?

The study is being organised by Professor Mona Bafadhel, funded by a research grant from AstraZeneca. The study is sponsored by the University of Oxford. During the study, we would like to keep you informed of the results of the study and will send you a newsletter with this information and further updates. We will provide you with a contact card for the study team and information about the study you are undertaking.

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by 20/LO/0187.

Participation in future research

We would like the opportunity to contact you for participation in future studies that may be of interest to you. Agreeing to this, does not mean you have to take part. If you do agree to be contacted in the future, your personal details will be stored in a secure, password-protected database at the University of Oxford and only accessed by delegated members of the research team.

Thank you for taking the time to read this information

Please ask if you have any further questions

Study assessment information

Measuring oxygen levels (10 seconds): A probe will be placed on your finger to record your oxygen levels.

Measuring your temperature (30 seconds): An aural (ear) or oral (mouth) probe will be used to test your temperature.

Measuring your blood pressure (30 seconds): A cuff will be placed around your arm to measure your blood pressure.

Recording your heart tracing (60 seconds): The electrical activity of your heart will be measured in the form of an ECG. Sticky pads are placed in areas across your chest, arms and legs and a trace is recorded.

Questionnaires (5 minutes total): The questionnaires are designed to measure your overall health, symptoms and quality of life. There will be up to 5 questionnaires to complete. The study team will go through each questionnaire and answer any questions you may have.

Breathing tests (3 types): **Test 1** - Exhaled Nitric Oxide (10 seconds). You will be asked to take a deep breath and then blow into a machine for 10 seconds. This will measure inflammation in your breath. **Test 2 -** Spirometry (3 minutes). You will then be asked to blow into a machine up to 3 times to measure the capacity of your lungs. This is called spirometry and includes a peak flow test. **Test 3 -** Impulse oscillometry (5 minutes). At normal breathing rates, you will be asked to breathe into a mouthpiece with a nose clip on connected to a special device. The device sends vibrations to measure how stiff the large and small air tubes in the lungs are.

Chest x-ray: If you have not had an x-ray in the last 12 months, or it is felt to be clinically indicated when we see you, we will organise this as part of standard clinical care.

Blood tests (2 minutes): A maximum of 65mLs (5 tablespoon equivalent) will be taken at each visit. This blood collected into anonymised tubes and transported to the John Radcliffe Hospital. This will also include the measurements of the eosinophil level.

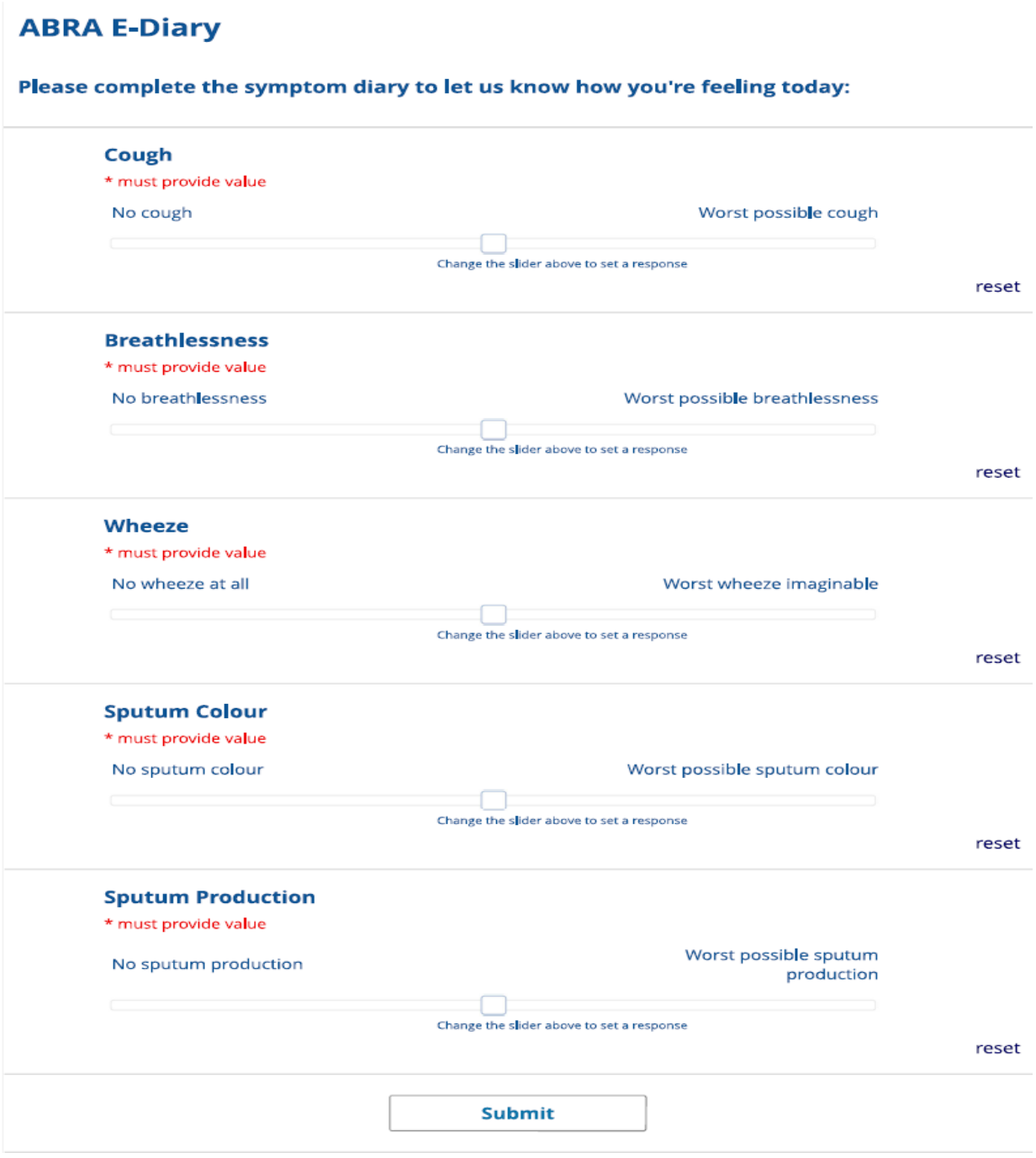
Sputum testing (5 minutes): Sputum (phlegm) is collected spontaneously (a sample that you simply cough up) or can be collected via the sputum induction method. This involves breathing in a salty-water mist, via a nebuliser to help you cough up the phlegm. Breathing tests will be performed to make sure your lungs are not irritated by the salty-water mist. Salbutamol (Ventolin, a reliever inhaler) will be given to help if this is required.

Symptom diary card (2 minutes): We will ask you to complete a diary of your symptoms on an electronic tablet daily up to and including 28 days after an exacerbation. An alert will be set up for 3 days after you have study medication. This is to inform the study team if your symptoms are not improving as well as we expect.

Urine testing: A sample of urine will be tested for levels of protein, sugar and any signs of infection or pregnancy. This will then be discarded.

Electronic diary card: We will provide you with an electronic tablet for you to fill in and complete daily symptoms for the first 28 days after your exacerbation (visit 2). You will be allocated a study specific e-mail address at visit 2. Study staff will help you set up the

electronic device. You will then receive a unique e-mail with a link to your electronic diary on a daily basis. Click on the link and you will see a diary screen as shown below. The diary will assess 5 different symptoms. For each symptom, use your finger to slide the marker on the scale._When complete, please tap on the 'submit' button._For the first 3 days, if your symptoms deteriorate, the electronic diary will alert the study staff to contact you. If you yourself feel worse, please call the study staff at any time.



Contact details:

Chief Investigator: Professor Mona Bafadhel, Associate Professor Respiratory Medicine & Honorary Consultant Chest Physician, Respiratory Medicine Unit, Nuffield Department of Clinical Medicine, University of Oxford, Old Road Campus, Oxford OX3 7FZ.

	Study Doctor	Study Nurse (s)
	Dr Sanjay Ramakrishnan	Miss Christine Mwasuku
Direct telephone	07468 340 248	07468 340 248
Telephone. Via hospital system	01865 225 759	01865 227 242

This study will form part of Dr Sanjay Ramakrishnan's higher degree by research (PhD).

Email: ABRA@ndm.ox.ac.uk