NIHR Southampton Clinical Research Facility
University Hospital Southampton NHS Foundation Trust
C Level West Wing, Mailpoint 218
Southampton
SO16 6YD
Tel: 023 8120 4479
Email:Respiratory.Research@uhs.nhs.uk
Website: www.southamptoncrf.nihr.ac.uk

Patient Information Sheet

seASonal asthma exaCerbation prEveNtion with Depemokimab

(ASCEND)

Chief Investigator: Professor David Jackson

- We would like to invite you to take part in a research trial (also called a research study).
- Before you decide whether you would like to take part in the trial, it is important that you understand why the research is being done and what it would involve for you.
- Please take some time to read the information carefully, and if you would like to, discuss with your family, friends and doctor.
- Please feel free to talk to us if anything is not clear, or you would like more information.

Thank you for taking the time to consider taking part in the ASCEND Study.

How to contact us:
Local Research Team Contact: Elizabeth Holliday **Email:** RespiratoryResearch@uhs.nhs.uk **Telephone Number: 023 8120 4479**

Key information

- This study is testing a drug called depemokimab which will be given once as an injection. You may receive this drug or a placebo.
- The study will test whether depemokimab can help reduce asthma attacks in autumn/winter time, in addition to the asthma medication you already take.
- Depemokimab is an experimental drug. This means it is still being tested in clinical trials and is not available to doctors to prescribe to patients yet.
- In this study there are six study appointments (visits) over around eight months, either face to face, by video conference, or by telephone.
- During these visits, tests and procedures including blood tests, electrocardiograms, and lung function tests, will be done. You will also be asked to complete questionnaires about your health, asthma and your treatment.
- We plan to recruit 170 participants into this trial by autumn/winter this year.
- We will reimburse you for your time and your travel expenses.
- If you are pregnant, breast feeding, or planning to get pregnant, you are not able to take part in the trial.
- Your health and wellbeing will continue to be our priority. Therefore, if you take part in the trial but your doctor feels that your treatment needs to be changed, they will do what is best for you, regardless of trial participation.
- KCL and Guy's and St Thomas' NHS Foundation Trust are collaborating with a company called GlaxoSmithKline to deliver this study. GlaxoSmithKline are funding the study.

In this Patient Information Sheet:

This information sheet explains why this trial is needed and how we are planning to do it. It contains details on how we are using the information we collect about you and who has reviewed and approved the research.

You will also find information on what you will need to do if you decide to take part, as well as the risks and benefits to you.

A member of the research team can go through this information sheet with you at any time, and as many times as you wish, to help you decide whether or not you would like to take part in the trial.

As this study aims to reduce the pressure hospitals are under to treat seasonal illnesses during the autumn/winter period, recruitment to this trial needs to be completed quickly. This means that we will always give you as much time as possible to read through this information, but we are aiming to complete recruitment in four to six weeks. So the opportunity to take part is limited to this time.

1 Why is this research needed?

Respiratory infections caused by viruses, such as the cold and the flu, are a major cause of asthma attacks (also called exacerbations). During autumn and winter, asthma attacks are more common and cause a great deal of suffering for asthmatic patients. Visiting the hospital for treatment for asthma attacks during this time of year is also much more common.

Respiratory viral infections can cause the airways in the lungs to swell up and produce mucus, which can trigger an asthma attack.

Airway swelling happens because your body produces more eosinophils. Eosinophils are a type of white blood cell, and a normal part of your immune system.

The aim of the ASCEND trial is to find out if depemokimab, as an add-on treatment can help reduce seasonal asthma attacks during autumn and winter, by reducing the number of eosinophils in your body.

To do this, we are aiming to make sure all participants are recruited to the trial by autumn/winter this year.

2 What is the drug being tested?

Depemokimab is a type of medicine called a monoclonal antibody and it works by reducing the number of eosinophils in your body. Depemokimab blocks interleukin-5 (IL-5), a protein made by white blood cells. IL-5 is responsible for the growth and development of eosinophils.

Depemokimab has been designed to work against IL-5 for six months, (covering the entire autumn and winter period). It is available as a subcutaneous injection. Subcutaneous means that the injection goes under the skin (and not into a vein or muscle).

The placebo does not contain any medicine or drug. It is a saline solution, which is a mixture of water and salt.

3 What type of trial is this?

This trial is a phase 3B clinical trial or study. It means the study drug, is being tested for how safe it is and how well it works when taken with standard of care asthma medication. Depemokimab has been tested in other clinical trials in asthmatic patients but it is currently not available for doctors to prescribe it to their patients.

4 How will the study work?

We will invite 170 patients to take part in the ASCEND trial across eight hospital sites in the UK.

During the trial, all participants will receive one subcutaneous injection. Half of the patients will receive the study drug, depemokimab and the other half will receive placebo.

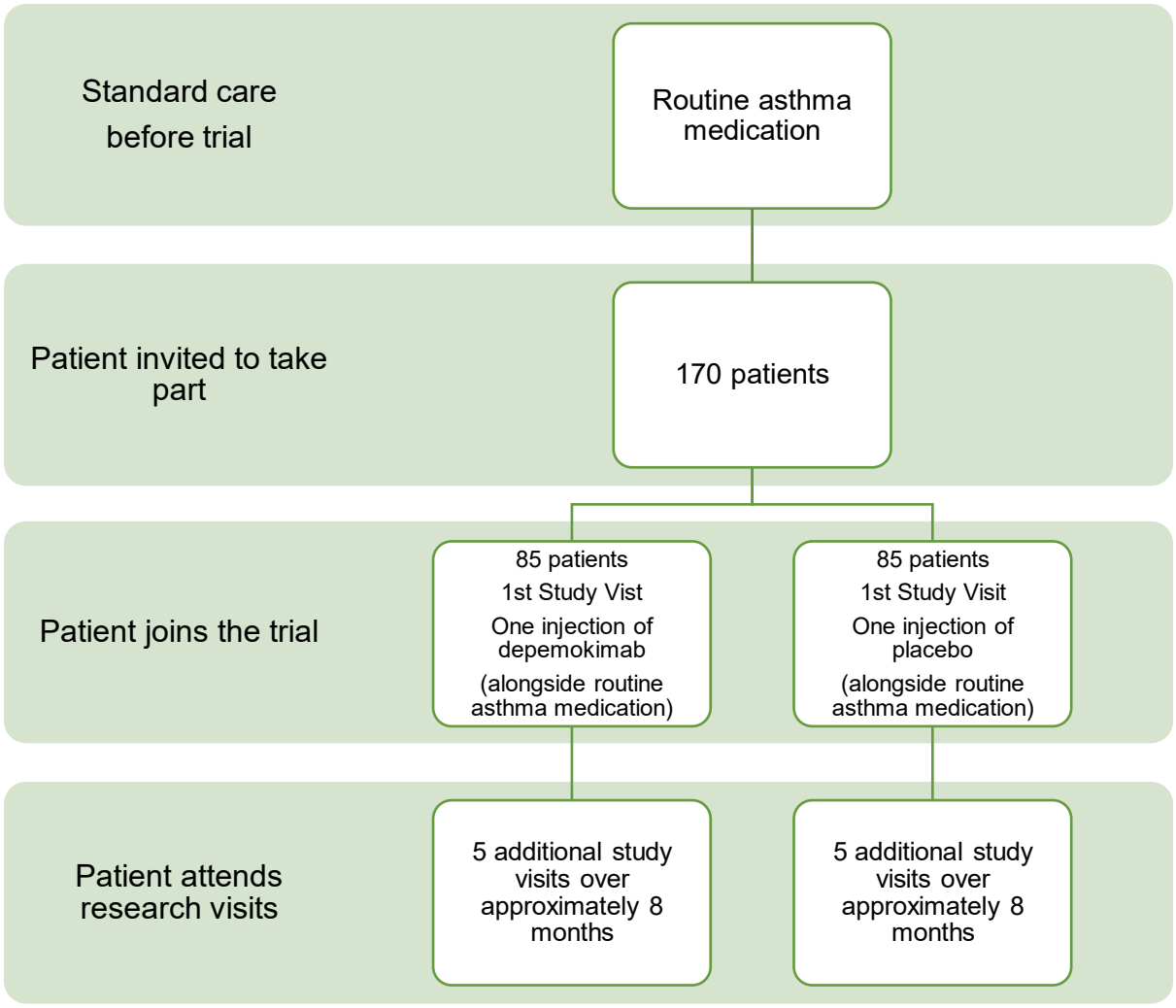
Whichever group you're in, you will continue to use your standard of care asthma inhaler and asthma medication.

There is an equal chance of being in either group. A computer programme will decide if you receive the depemokimab or the placebo, a bit like rolling dice or flipping a coin. This is called randomisation.

You will not know which group you have been assigned to, and neither will your doctors and nurses. However, the doctors can find out if they need to. This type of study is called a randomised, double-blind trial.

The study will last for around eight months and you will be asked to complete six study visits during this time. At end of the study, the effects of treatment with depemokimab will be compared to the placebo.

A diagram of the patient pathway is shown below



5 Why have I been invited to take part?

You have been invited to take part in this research trial because you have moderate to severe asthma. Your asthma care team think you might be suitable to take part in this trial.

6 Do I have to take part?

No, taking part in this study is completely voluntary. It is up to you to choose whether or not you would like to take part.

If you decide to take part in the trial you will be given this information sheet to keep and be asked to sign a consent form. You are still free to leave the study at any time and without giving a reason. Leaving will not affect your care or your legal rights. If you choose to leave the study, please let your study team know as soon as possible.

If you decide not to take part in the trial, you will continue to receive care for your asthma. If you agree, we would still like to collect follow up information to see how you are feeling.

7 What will I need to do if I take part?

If you agree to take part you will be involved in the study for around eight months from signing the consent form to the last research visit.

You will be asked to complete six research visits.

The first visit is called the screening visit and it will take place at your local hospital, like an outpatient appointment. At the screening visit we will check that you are eligible to be in the study. If you are eligible we will give you the injection of either depemokimab or placebo at this visit.

You will also be asked to attend five study visits at four, 10, 18, 26 and 35 weeks. The research team will arrange the visits at times that are convenient for you.

Some of the research visits will be face to face at your local hospital. Some of the visits will be remote and the study team will call you by telephone or by a video call.

Research visits are similar to a clinical outpatient appointment, but you will be asked to have additional tests and procedures to help answer the research question. You will also be asked to complete questionnaires about your health and asthma.

You will be given a patient contact card with emergency contact details for the study. You should try and carry this with you at all times and show it to a doctor if you are admitted to hospital.

Whilst you are taking part in this study you should tell the study doctor of any medications you take, including over-the-counter medicines and vitamin supplements. Your doctor will discuss any drugs that you should not take during the study.

We will let your GP know you are taking part in the trial. If anything comes up in the trial which may be important for you and your GP to know, we will inform both you and your GP.

8 Will I be reimbursed for taking part?

Yes. you will receive £100 for each completed face-to-face visit up to a maximum of £300 for all face-to-face visits attended. In addition, we will reimburse any travel expenses incurred.

9 Will I have to give samples?

Yes, we will take samples from you. Some of these are part of your standard clinical care and you will have had them before.

What samples will I have to give?

We will ask you to give the following samples:

- **Blood samples** The blood tests will allow us to check that it is safe for you to take part in the study and to see if the study drug works.
    - An extra blood sample will be needed if you have visited a country that is at high risk for parasitic infections (such as malaria) within six months of a study visit

The total volume of blood that you will be asked to give during the main study is expected to be about 4 tablespoons (about 65 millilitres or mL). Extra blood may need to be collected from you if you visited a country that is high risk for

parasitic infection (see above), for safety reasons, or due to any technical issues with the samples.

- **Urine samples (if you are female)** Urine will be collected from women who are able to become pregnant, to test for pregnancy.

10 What will happen at the research visits?

Research visit 1: Screening and randomisation

At your first research visit, you will have the opportunity to ask any further questions you may have about the trial. If you are happy to take part, you will be asked to sign a consent form confirming that you understand the trial and you agree to take part. You will be given a copy of the signed consent form.

The following procedures will be done by the study team, to make sure that you are eligible for the trial. A full list of criteria must be met in order for you to take part. This is to ensure that it is safe and appropriate to enrol you in the trial, before you are given the study drug or placebo injection.

- Medical examination, including vital signs. We will check your blood pressure, heart rate, temperature, respiratory rate and oxygen saturations) as well as your height weight, and BMI (body mass index).
- Collection of relevant medical, asthma, smoking history and medications you take (including Rescue Medication Use or quick-relief asthma medicines you have used)
- An electrocardiogram to measure the hearts electrical activity. 12 sticky tabs called electrodes will be applied to your chest and limbs. Cables from an ECG machine will be attached to the tabs, and the ECG machine will measure electrical signals from the heart. The ECG is a painless test but you might feel some discomfort when the sensors are removed (a bit like removing a plaster).

- A breathing test called Spirometry: You will be asked to breathe into a tube attached to a machine in order to measure how well you breathe. During the procedure, you will be given a bronchodilator (an inhaled drug to open your airways). Spirometry is a straightforward test although some people may feel dizzy, faint, shaky, sick or tired for a short period afterwards. The test may take 30-90 minutes.

  Before this test you will need to:

  - **refrain from** strenuous exercise for at least 30 minutes prior to the test
  - **avoid** eating a large meal for at least two hours prior to the test.

- A lung function test - Fractional exhaled nitric (FeNO) oxide breath test is used to measure inflammation in your airways. You will put in a mouthpiece that's attached to a tube that leads to an electronic measurement device. You will exhale slowly in order to determine the amount of nitric oxide in your breath, for approximately 10 seconds. Nitric oxide can indicate the level of inflammation in your lungs.

  Before this test you should:

  - **avoid** smoking at least one hour before the test
  - **avoid** hot drinks, caffeine, and alcohol for at least one hour before the test
  - **avoid** eating foods such as green leafy vegetables and beetroot for at least three hours before the test.

  You can take your regular medicines as usual before the test. The FeNO test is considered safe and easy to conduct.

- Collection of blood samples: we will collect your blood by venepuncture (also known as phlebotomy or a blood draw) which involves inserting a sterile needle into one of your veins (usually in the arm or hand) and collecting the blood into a vial.

- Questionnaires: You will be asked to complete two types of questionnaires (Asthma Control Questionnaire, ACQ-5 and Asthma Quality of Life Questionnaire, AQLQ(S)+12) about your asthma symptoms, how your asthma affects your life, and about how you feel about your treatment.

- Health care utilisation: Your study team will ask you questions about any visits you have made to the GP or hospital for asthma treatment, and any medications given to you.

If you are a woman and there is a chance of you becoming pregnant you will have a blood and urine pregnancy test at this visit. You will be asked to attend an additional screening visit on another day to review the results before receiving the injection.

If you are a women who is able to become pregnant you must be using a highly effective form of contraception method to avoid pregnancy. You must have been using the contraception for at least 14 days before you receive the injection and throughout the trial including the last study visit. The study doctor will confirm for how long you need to use highly effective contraception when you leave the study.

Highly effective forms of contraception include:

- Combined (estrogen and progestogen containing) hormonal contraception such as:
    - Oral pill
    - Vaginal ring
    - Transdermal patch
- Progestogen-only hormonal contraception such as:
    - Oral pill
    - Injection
    - Implant
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion
- Vasectomised partner

- Abstinence

If you became pregnant during the trial you must inform your trial doctor immediately. You can ask to find out if you were randomised to receive the study drug or placebo. This is called unblinding.

- If this takes place *before* completing the week 26 visit, you will not be able to continue in the study. You will be monitored during your pregnancy until birth and we will ask you questions about you and your baby's health.
- If you are unblinded *after* the week 26 visit, you can complete the final follow up visit in addition to the monitoring of your pregnancy until birth and questions about you and your baby's health.

If you are a man you must be using an effective form of contraception (condoms) to avoid pregnancy until after the last study visit (week 35).

If you are eligible to participate you will receive the injection on the same day. You will receive one single dose of either 100mg of the depemokimab or 100mg of the placebo, by subcutaneous injection.

You will be monitored for a minimum of 2 hours after receiving the depemokimab or the placebo to check for any side effects.

If the study team decide that it is not safe for you to take part in the study, we understand any disappointment you might feel. Your time and willingness to complete the screening visit is valued. It will help the study team to identify common reasons why people may not be able to participate, which in turn will improve the recruitment process for the study.

Below is a list of all the tests and procedures that will happen at visit 1:

Time point	Type of Visit	Tests/procedures
Visit 1 Week 0	**Screening and Randomisation.** **Outpatient visit at your local hospital.**	Screening • Sign consent form • Medical history • Asthma attack history • Physical examination • Vital signs • Blood tests (about 4 teaspoons or 20 mL) • Pregnancy test, blood and urine, for women who could be pregnant • 12 Lead ECG • Lung function tests (Spirometry and FeNo test) • Questionnaires • Health care resource review • Confirmation of eligibility by trial doctor Randomisation • Subcutaneous injection of depemokimab or placebo. • Minimum 2-hour observation

Research visits 2, 3, 4, 5, and 6

Below is a list of all the tests and procedures that will happen at visits 2, 3, 4 , 5 and 6:

Visit 2 Week 4	**Remote visit by telephone or video call**	• Medication review • Rescue medication use review (quick relief medication) • Asthma attack history • Questionnaire • Health care resource review
Visit 3 Week 10	**Remote visit by telephone or video call**	• Medication review • Rescue medication use review • Asthma attack history

	AND **One outpatient visit at your local hospital or your GP**	• Questionnaire • Health care resource review Outpatient visit • Blood tests (about 1 teaspoon or 5 mL) (This may include a pregnancy test, women who could become pregnant)
Visit 4 Week 18	**Remote visit by telephone or video call**	• Medication review • Rescue medication use review • Asthma attack history • Questionnaire • Health care resource review
Visit 5 Week 26	**Outpatient visit at your local hospital.**	• Medication review • Rescue medication use review • Asthma attack history • Blood tests (about 4 teaspoons or 20 mL) (This will include a pregnancy test for women who could become pregnant) • Lung function tests (Spirometry and FeNo test) • Questionnaires • Health care resource review
Visit 6 Week 35	**Outpatient visit at your local hospital.** **End of study**	• Medication review • Rescue medication use review • Vital signs • Blood tests (about 4 teaspoons or 20 mL) (This will include a pregnancy test for women who could become pregnant) • 12 Lead ECG • Lung function tests (Spirometry and FeNo test) • Questionnaires • Health care resource review

11 What will happen to my samples?

Blood samples will be processed at laboratories at your local hospital.

All the samples will be labelled by hospital staff using your initials and a code that can only be linked to you by the study team at your hospital. You have the right to

request samples collected as part of this study be destroyed and no further laboratory analysis to be performed if you decide to withdraw from the trial.

12. Will my samples be used in future research?

No, your samples will be discarded once they have been processed.

13. What are the possible benefits of taking part in the study?

It is possible that depemokimab will reduce your asthma attacks during the autumn and winter time. However, we cannot say this for certain until we have completed this, and future studies. If you are given the placebo injection, you will not be receiving a drug that could potentially help with your asthma attacks. You may not directly benefit from taking part in this study, but the information gained from your participation may help to improve the treatment of patients with your condition in the future.

14. What are the possible risks of taking part in the study?

There is a possibility that you may still have asthma attacks during the study.

It is possible that some patients could have side effects that we do not know about yet.

Possible side effects of depemokimab

- Very common side effects (these may affect more than 1 in 10 people): Headache

- Common side effects (these may affect up to 1 in 10 people):

  Chest infection (symptoms of which may include cough and fever [high temperature]); urinary tract infection (blood in urine, painful and frequent urination, fever, pain in lower back); upper abdominal pain (stomach pain or discomfort in the upper area of the stomach); fever (high temperature);

eczema (itchy red patches on the skin); injection site reaction (pain, redness, swelling, itching, and burning sensation of the skin near where the injection was given); back pain; pharyngitis (sore throat); nasal congestion (stuffy nose)

- Rare side effects (these may affect up to 1 in 1,000 people):

  Allergic reactions, which may be severe (such as anaphylaxis)

  You will be monitored closely while you receive the study drug and for two hours afterwards, and if a reaction occurs, the doctor may decide to give you treatment to reduce the severity of side effects. In rare circumstances, this allergic reaction can be life threatening (called anaphylaxis).

  Seek medical attention immediately if you think you are having an allergic reaction.

  Symptoms of allergic reaction can include

  - Swelling, sometimes of the face or mouth (angioedema)
  - Becoming very wheezy, coughing or having difficulty breathing
  - Suddenly feeling weak or light in the head (may lead to collapse or loss of consciousness)
  - Skin rash (hives) or redness

Call the study doctor right away if you

- Feel very tired or faint
- Have pain or feel sick in the stomach and do not want to eat
- Have chest pain, tightness or palpitations (an abnormal awareness of the heart beating fast or skipping beats)
- Have yellow eyes or skin or dark urine
- Bruise more easily or develop itching
- Become confused

Risks associated with the procedures

- Subcutaneous injection of depemokimab or placebo – pain, redness or bruising at the site of the injection.
- Collection of the blood samples – you may experience discomfort and there is a risk of bleeding and bruising around the puncture site but this is very rarely serious.
- ECG – small sticky pads are applied to certain parts of your body. Some areas on which the patches are placed may need to be shaved. You may also feel a small amount of irritation, itching, or redness on the skin after these pads are removed. This should disappear in a few days.
- Spirometry (breathing test) – you may temporarily have mild chest tightening, coughing (worsening of asthma symptoms), shortness of breath, dizziness, or feel faint. The fast-acting airway-opening medication, called "bronchodilators", used during some breathing tests, is the same type of medication that you use at home to treat sudden asthma symptoms. This type of medication may cause fast heart rate, nervousness, or shakiness

15. What happens if something goes wrong?

If you become ill or are injured while you are in this research study, you must tell your study doctor straight away.

If you need to report side effects or are feeling unwell, please contact the study team telephone number on the patient contact card you have been given.

Office hours: 02381 204479

16. What happens when the study stops?

You will return to the care of your local doctor (GP) and the hospital doctors you would see routinely to continue with your usual care.

17. What will happen to the results of the study?

The results from this study will not be known until the trial is completed. It is expected that the trial will last nine months in total. We are hoping to publish the results through medical publications and presentations shortly after completing the study. At this point, we will be happy to send you a summary of the study results at your request. For this we will ask you to provide a postal or email address to your research team and your preference will be noted on your Consent Form. You will not be identifiable in the report.

All clinical trials need to be registered in public databases to make the research transparent. Therefore, information about this research and its results will be published in a research registry called ISRCTN https://www.isrctn.com/.

18. How will we use information about you?

We will need to use information from you and your medical records for this research project. This information will include your:

- Name
- NHS number (England) or Community Health Index CHI (Scotland)
- Initials
- Contact details
- Hospital number.

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, NHS number, hospital number, or contact details. Your data will have a code number instead.

King's College London (KCL) and Guy's and St Thomas' NHS Foundation Trust are the co-sponsors of the study and will keep all information about you safe and secure.

Information about the possible side effects depemokimab will be collected during the study. This information will be shared with the company who is providing the study drug, called GlaxoSmithkline. Your personal details will not be shared.

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 a way that no one can work out that you took part in the study. We will keep your study data for a maximum of 25 years. The study data will then be fully anonymized and securely archived or destroyed.

19. 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 your hospital. If you do not want this to happen, tell us and we will stop.

You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. 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 study, you will have the option to take part in future research using your data saved from this study.

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

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

- Asking a member of the research team (contact details included below)
- Sending an email to RespiratoryResearch@uhs.nhs.uk

- Ringing us on 023 8120 4479
- Visiting the Health Research Authority website 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/

- Visiting the Guy's and St Thomas' website at www.guysandstthomas.nhs.uk/research/patients/use-of-data.aspx

  and

  Visiting King's College London website at: https://www.kcl.ac.uk/research/research-environment/rgei/research-ethics/use-of-personal-data-in-research

- By contacting the Data Protection Officer: dataprotection@uhs.nhs.uk (For GSTT: Nick Murphy-O'Kane DPO@gstt.nhs.uk; For KCL: Elizabeth Powis info-compliance@kcl.ac.uk)

MORE INFORMATION ABOUT THE STUDY

21. What if new information becomes available?

Sometimes during the course of a research study, new information becomes available about the medication that is being studied. If this happens, we will tell you about it and you can discuss whether you want to continue in the study.

The study doctor can also choose to take you out of the study if they believe that is what is best for you.

22. What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the study doctors and nurses at your local hospital, who will do their best to answer your questions.

If you remain unhappy and wish to complain formally, you can do this through the Patients Advice and Liaison Service (PALS) on 023 8120 6325, email pals@uhs.nhs.uk.

In the event that something does go wrong and you are harmed during the research and this is due to someone‘s negligence then you may have grounds for legal action for compensation against Guy’s and St Thomas’ NHS Foundation Trust and/or King’s College London, but you may have to pay your legal costs. The normal NHS complaints mechanisms will still be available to you (if appropriate).

23. Who is organising and funding the study?

The study has been organised by the Asthma Centre at Guy’s and St Thomas’ NHS Foundation Trust. The study is co-sponsored by King’s College London and Guy’s and St Thomas’ NHS Foundation Trust.

The trial is funded by a company called GlaxoSmithKline.

24. Who has reviewed the study?

This research has been reviewed by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by East Midlands – Nottingham 2 Research Ethics Committee. The study has also been reviewed by the UK Regulatory Authority, the MHRA (the Medicines and Healthcare products Regulatory Agency). The MHRA is part of the Department of Health with the responsibility to regulate clinical trials of medicines in the UK

Asthma patients were involved in reviewing and providing feedback on this Patient Information Sheet, the Patient Invitation Letter and Informed Consent Form.

Thank you for taking the time to read this Patient Information Sheet.

If you have any questions or would like to discuss the study further, please contact your local research team:

Principal Investigator at your hospital (local research team):
Principal Investigator: Dr Hitasha Rupani
Email: RespiratoryResearch@uhs.nhs.uk
Tel: 023 8120 4479