



A randomised placebo-controlled trial of anti-ST2 in COPD (COPD-ST₂OP)

PARTICIPANT INFORMATION SHEET

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Invitation

You are being invited to take part in the above research trial because you have chronic obstructive pulmonary disease (COPD). Before you decide whether to take part it is important for you to understand why the research is being done and what it involves. Please take time to read this information sheet and discuss it with others if you wish. If there is anything that you do not understand, or you require further information on, please contact us and we will be happy to speak to you.

What is the purpose of the trial?

Chronic obstructive pulmonary disease (COPD) is a significant cause of morbidity and mortality worldwide and it is associated with acute exacerbations (sudden worsening of COPD symptoms) which can lead to hospitalisation. This trial is comparing Anti-ST2, an experimental and currently unlicensed drug, with a placebo (a substance containing no active medication) to treat COPD with the aim of reducing the number of exacerbations of the disease. In order to understand the underlying mechanism(s) of COPD exacerbation we would like to collect and analyse samples of blood, sputum, breath, urine and undertake measurements of lung function (breathing tests) and a CT scan of the chest. You will then either receive treatment with the trial drug (Anti-ST2) or the placebo.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form. If you decide to take part you are free to withdraw from the trial at any time and without giving



a reason. If you do not take part, or if you withdraw from the trial, this will not affect the standard of care you receive.

What will happen to me if I take part?

We will ask you to come to the appointments at the Respiratory BRC (Biomedical Research Centre) at Glenfield Hospital. You will have an initial screening and consent visit, after which you would return for 12 scheduled treatment visits spread over the next 44 weeks (~1year) and 2 final follow up visits at 48 and 60 weeks (15 scheduled visits in total). At the initial screening and consent visit the trial doctor will explain the details of the trial. If you agree to take part, you will be asked to sign the consent form.

Visit Schedule	Approx duration
Screening (visit 0) Consent, review of eligibility criteria, demographics, weight height, medical history, smoking history, drug history, vital signs, physical exam, Sputum sample, blood tests, urine sample, breath and nasal samples, lung function test, pregnancy test (if indicated), ECG, CT chest, collect participant diary	4 hours
Visits 1, 2, 4, 7 and 10 Review of medications, review of eligibility criteria, physical exam Vital signs, 4 questionnaires ECHO (if indicated), sputum sample, blood and urine samples, pregnancy testing (if indicated), collect participant diary Randomisation to drug or placebo (visit 1 only), infusion of drug or placebo	3 hours
Visits 3, 5, 6, 8, 9, 11 and 12 Vital signs, review of medication, review of eligibility, pregnancy testing (if indicated), collect participant diary, infusion of drug or placebo	2 hours
Visit 13 Review of medications, review of eligibility criteria, vital signs Collect participant diary, sputum, blood, urine, breath and nasal samples Spirometry, pregnancy testing, 4 questionnaires	2 hours



Visit 14 (washout) Review of medications, review of eligibility criteria, vital signs Collect participant diary, pregnancy testing, physical exam, ECG, CT chest 4 questionnaires, sputum, blood, urine, breath and nasal samples	2 hours
Withdrawal Review of medications, review of eligibility criteria, vital signs Collect participant diary, sputum, blood, urine and nasal samples Spirometry, pregnancy testing	2 hours
Unscheduled visit (e.g. exacerbation) Review of medications, review of eligibility criteria, vital signs, spirometry Collect participant diary, physical exam, ECG, ECHO (if indicated), chest x-ray, pregnancy testing (if indicated), sputum, blood, urine, breath and nasal samples	2 hours

The tests you may be asked to perform at the screening visit are outlined below, you may be asked to participate in any single procedure or combination of procedures on these visits. In the majority of visits we will not perform any tests other than measuring your vital signs (heart rate, oxygen saturation, blood pressure, respiratory rate, temperature) and the delivery of the trial drug:

- **Medical history, demographics (e.g. age, gender), vital signs, physical examination and questionnaires:** We will ask you about your previous medical history and any current medical problems that you may have. A doctor will perform a physical examination (listen to your heart and lungs). We will ask you about medications that you are taking and a record of your smoking history. You will be asked to fill in questionnaires regarding your respiratory symptoms. We will ask your consent for trial personnel to view relevant sections of your medical records held by the hospital or your GP practice.
- **Sputum Collection:** We will analyse your sputum sample in the laboratory to measure the types of cells, inflammatory chemicals and organisms in it. If you cannot bring up any sputum you may need to



inhale a salty solution. This test is called sputum induction. For this test we will perform spirometry (lung function test) as a safety measure, followed by inhalation of Ventolin (salbutamol) or equivalent. Once we have your spirometry measurements you will then inhale the salty solution followed by repeat spirometry a few minutes later to ensure it has not affected your lung function. This test can cause some chest tightness, wheezing and/or cough. These can all readily be reversed by inhaling Ventolin (salbutamol). Sputum will be collected on most but not all visits. If your lung function test indicates severe disease then we will not perform the sputum induction.

- **Blood Collection:** You will be asked to provide no more than 100 ml of blood (equivalent to 10 tablespoons) at screening (Visit 0), Visit 1, Visit 2, Visit 4 and then 12 weekly (~every 3 months) until Visit 14 at Week 60. However the amount usually required is half this. This may cause some mild discomfort and occasionally some bruising. These blood tests will assess your kidney, liver and heart function, fats and sugar levels, allergies, inflammation, whether you have anaemia, how your body reacts to the drug/placebo and pregnancy (if applicable). All participants will be asked to undergo the blood tests.
- **Breathing Tests:** This will involve breathing out as hard as you can several times, repeated once more after inhaling Ventolin (salbutamol) or equivalent (Spirometry). Other tests involve breathing in safe gas mixtures and blowing tests to measure how well your lungs are working. There is also a breathing test carried out with you sitting in a transparent glass booth and others where we collect breath samples. Other simple breathing tests may also be performed. The breathing test may cause some temporary light headedness and coughing. Lung function/breathing tests are not guaranteed to happen at each visit for various reasons such as faulty equipment, lack of trained staff, or if you refuse to undergo the test.
- **Nasal sampling:** A small brush or scoop is inserted and gently rubbed inside the nostril. This takes a few seconds to do. There may be a little discomfort that induces sneezing, coughing and, rarely, minor bleeding for a short period of time. A small piece of paper will be inserted into the nostril to collect nasal fluid.



- **Urine sample:** A sample of urine will be collected to test for inflammatory markers and as a secondary pregnancy test if indicated in women of child bearing potential.
- **Pregnancy Tests:** Due to the nature of this trial, women who are pregnant, breastfeeding or who intend to become pregnant would not be eligible to take part. To be eligible to participate, women of child-bearing potential must have a negative blood pregnancy test performed at the screening visit and must agree to use two methods of birth control, (one of which must be a barrier method) for the duration of the trial. Men will also be required to discuss adequate forms of contraceptive during their participation in this trial. This is for safety reasons as the effects of the trial drug on an unborn foetus have not yet been determined. If you or your partner become pregnant during the trial, we will liaise closely with obstetricians and your GP to monitor the pregnancy.
- **CT Scan:** CT stands for 'computed tomography' and is a sophisticated type of X-ray. You will lie on a bed under a scanner and will be asked to hold your breath briefly. The amount of radiation involved is very low and we will take all safeguards to minimise the amount of x-rays you receive (please see the separate patient information sheet for further details). If you are claustrophobic or unable to lie flat, you do not have to undergo a CT scan.
- **Electrocardiogram (ECG):** is a simple painless test, with multiple electrodes (wires) used to record electrical activities of the heart. A wire is attached to each ankle and wrist with sticky pads and the remainder attached to the chest. You will be asked to lie on a bed and to relax for a few minutes before the recording is made. This test does not hurt, however it may cause minor discomfort during the removal of the ECG stickers from your chest. Very rarely someone may have a slight skin reaction to the stickers, but normally there are no after effects.
- **Daily diary:** we will ask you to contact the trial team and record any changes to your health or medication, in a participant diary reviewed at each visit. This would include any appointments with healthcare professionals, accidents, worsening (exacerbations) of your COPD or possible side effects of your trial drug, for safety purposes.



Will any genetic tests be done?

Genetic Testing (DNA): A blood sample will be collected for genetic testing to investigate whether there are links between response to treatment for COPD and people's genetic make-up. This test is optional. You and your GP will not receive individual results from these tests as they are not being used for diagnostic purposes, they are solely for research and safety purposes. All genetic samples and tissue samples taken for this trial will be anonymised and will be destroyed either during or after analysis (no longer than 25 years after the end of the trial).

How many visits will I need to attend?

After the initial screening visit (Visit 0) you will attend Visit 1 (baseline) and would be allocated one of the two treatments randomly by a computer system, therefore there will be a 50:50 chance of continuing the trial treatment with either the Anti-ST2 or the placebo (you are not able to choose). However neither you, nor the clinical team administering the treatment will be told which treatment you are receiving, this is because the trial is double-blinded to help prevent bias and erroneous outcomes.

There will then be 12 treatment visits spread evenly every 4 weeks over a 44 week period (approximately 1 per month for 1 year). At these visits you will receive either the Anti-ST2 or the placebo via subcutaneous injection (injection under the skin) using an infusion pump during the visit. We will also perform a number of measures and repeat measures listed previously to assess your health and the effect of the treatment. If you experience an exacerbation we would ask you to contact the research team who will assess you and may arrange a chest X-ray, ECHO, ECG, blood, sputum and nasal sampling to assess your health and safety.

You will receive your final dose of Anti-ST2 or placebo at week 44, but will be followed up at weeks 48 and 60 to ensure that the treatment has left your system. This would mean that the whole trial after the initial screening visit, should take approximately 1 year and 3 months, spread over 14 planned trial visits, and any visits due to exacerbations.

Trial visits where we take detailed measures listed previously will take a maximum of 4 hours to complete (Screening, 1, 2, 4, 7, 10, 13, 14 and exacerbation). Treatment visits not involving tests other than vital signs and drug dosing should take approximately 1 hour to complete.



Will I be reimbursed or receive any payment for participating?

Once you have been allocated your treatment, you will be eligible to receive £25 for every completed scheduled trial visit (14 maximum). This can be paid either as a single amount at the end of the trial, or throughout the trial depending on your preference.

There is also a taxi service that can be provided to you should you require it, but we will also reimburse any travel and car park charges throughout the trial including for the initial screening visit and any exacerbation visits. These travel expenses will be paid at the usual NHS rate (45p/mile up to a maximum of £50 per return visit), so long as you retain and present your original receipts at the visit. Refreshments will also be provided during trial visits and a lunch provided during longer visits.

What do I have to do?

During the trial you will be encouraged to use your regular medication. Before visit 1 you will need to withhold certain inhalers, as these will affect the breathing tests. This is routine and you will be told about this during your telephone call with the research team before your first visit, you will also be given written information about this in your appointment letter.

Prescription of Drug Therapy?

The trial drug is known as Anti-ST2 (or MSTT1041A) given at 490mg under the skin by injection.

It is provided by Genentech who are funding this trial. This is being compared to a placebo ('dummy drug'). Once the trial has been completed you will no longer receive the trial medication either from your GP or the research team.

What are the possible benefits of taking part?

There are no guaranteed benefits to taking part in the study. If you are randomised to receive the Anti-ST2 we think that participants will experience a reduction in the number of exacerbations, but this is not certain.

During the trial irrespective of your randomised treatment, you will receive close monitoring of your condition to ensure that you are receiving the optimal medical treatment. Any exacerbations would also be investigated



and followed up by the trial team. Any abnormal findings arising from the trial procedures, that are considered to be clinically significant, would be managed either by the research team or reported to your GP for further investigation.

All participants taking part in this trial will also be helping to make significant contributions to research into COPD which may improve management of patients with this condition in the future.

What are the possible disadvantages and risks of taking part?

The trial is as low a risk as we can make it for a trial of this type. The effects and discomforts of each individual test are outlined earlier. Although some of the appointments with the full testing may be quite long (~4 hours), we will give you a break and provide refreshments.

We will ask you to withhold your inhalers before visit 1. There is a possibility that your symptoms may get worse for a short period of time. If that happens you should contact the research team. We will not be changing any of your medication, unless clinically indicated. You will also be able to contact a clinician from the trial by phone or email if you have any concerns in between your visits.

If you take part in this trial you will have two chest CTs which will be extra to those that you would have if you did not take part in the trial. If you experience any exacerbations the routine standard of care would also include a chest x-ray. These procedures use ionising radiation. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. We are all at risk of developing cancer during our lifetime. The normal risk is 0.5 (50% of the population at some point in their life will develop cancer). The two CT scans will increase your life time risk of future cancer by 0.1% to 50.01%. The chest x-rays at exacerbation visits have negligible radiation exposure.

Whilst the trial drug has undergone a number of early clinical trials which have had no safety concerns in asthma patients, this will be the first trial to look at participants with COPD. Therefore the full safety information on the drug is still unknown, but based on the results of other studies the current safety of the drug is considered good, with a slightly higher risk than you would receive from standard care.



Are there any side effects of the trial drug or placebo?

The majority of patients have not reported adverse reactions to the medication in the studies so far, however participants may experience some of the side effects listed below.

Side effects that have been noted in other early studies may include:

- headache, nose bleed, rash, tiredness, dizziness.
- Both the placebo and trial drug can potentially cause local Injection site reactions (e.g. redness, tenderness, bruising, swelling, itching, or infection) which may occur immediately but is usually short lived.

Rare side effects that may be more serious can also include:

- Immune responses or suppression and possible allergic reactions.
- Possible systemic reactions (e.g. skin rash, swelling, fever, chills, cough, wheezing and difficulty breathing, nausea and vomiting, sweating, chest pain, changes to your heart rate, and/or low blood pressure, which may require hospitalisation and medical intervention. This may occur within several hours of receiving the trial drug.

There are no identified risks associated with the Placebo which contains no active form of the medication. However on very rare occasions participants may react to the suspension fluid, which is similar to that of the trial drug (this is generally a harmless salt and sugar solution).

What if new information becomes available?

As part of this trial we may uncover medical conditions not previously recognised (e.g. abnormal liver test), if this happens we will assess your condition and manage you accordingly which may result in referral to other specialist teams or back to your GP for further investigations. If new safety information becomes available about the trial drug, we will let you know and will ask you to re-consent to the updated information.

What if something goes wrong?

It is very unlikely that you would be harmed by taking part in this type of research trial. However if you wish to complain or have any concerns about the way you have been approached or treated in connection with the trial, you should ask to speak to the local trial team on 0116 258 3370 who will do their best to answer your questions. If you remain unhappy and wish to address your concerns or complaints on a formal basis you should contact



Patient Information & Liaison Service or local complaints number on:
Freephone: 0808 178 8337; Fax: 0116 258 8661; Email: pils@uhl-tr.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 a legal action for compensation against University of Leicester but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my taking part in this trial be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. The University of Leicester is the sponsor for this trial. We will be using information from you and your medical records in order to undertake this trial and the sponsor will act as the data controller. This means that it is responsible for looking after your information and using it properly.

Consent forms and your participant ID (your unique identifier linked to your name) will be kept securely in an archive for 25 years as part of the research data so that the quality of the data can be verified if challenged.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the trial, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at <https://www2.le.ac.uk/colleges/medbiopsych/research/researchgovernance> or by contacting the trial sponsor on 0116 258 4099/258 4867 or uolsponsor@leicester.ac.uk.

During the trial, your samples and any data collected about yourself will be labelled with a unique participant ID, not your name. This number will be in place of any identifiable information. Only your trial doctor and some direct members of the trial team at the Respiratory BRC in Glenfield Hospital, will be able to link your participant ID to your name. The trial team at the Respiratory BRC, Glenfield Hospital will use your name, NHS number (if available) and contact details to contact you about the research trial, and make sure that relevant information about the trial is recorded for your



care, and to oversee the quality of the trial. Individuals from the University Sponsor, the Leicester Clinical Trials Unit (LCTU) who are managing the trial, the NHS Trust who are hosting the trial and regulatory organisations may look at your medical and research records to check the accuracy of the research trial.

The trial team at Glenfield Hospital will pass these details to the University Sponsor and/or the LCTU, along with the information collected from you and your medical records. The only people from the University Sponsor and the LCTU who will have access to information that identifies you will be people who need to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number, or contact details.

Your trial data will be stored on paper and on a secure computer database. These records will be kept separate from your medical records. Your medical records and previous tests performed to assess your respiratory condition (e.g. breathing tests) may be reviewed by research staff working on the trial for the purposes of research. This previously collected and prospectively collected clinical information may be utilised in an anonymised fashion for the purposes of research into asthma and COPD.

Your anonymised trial data may also be shared with our research collaborators in other academic institutions, industry partners and pharmaceutical companies. The Trial Doctor's institution and our research collaborators in other academic institutions and pharmaceutical research companies are each responsible for their handling of Trial Data in accordance with applicable Data Protection law(s).

The Hospital and our research collaborators in other academic institutions and pharmaceutical research companies may transfer Trial Data to countries outside of the UK and the European Economic Area (EEA) for the purposes described in this document. Please be aware that the laws in such countries may not provide the same level of data protection as in the UK and may not stop Trial Data from being shared with others. However, rest assured that all Trial Data that is transferred would be coded, so your identity is masked or made anonymous.

If you are deemed to be ineligible for the trial (even if this is prior to a screening visit 0), you will be 'screen failed' and your anonymised data



(initials and year of birth) will be added to a screening log along with the details of your ineligibility. You may still be contacted for future research.

Permission to contact your GP

Your GP will be notified of your taking part in this research. If you agree we will also contact your GP practice to request that its staff complete a questionnaire on your behalf about your medical history and COPD exacerbations, as well as any medications you are currently taking if required. The questionnaire labelled with your participant ID number, not your name, will be returned to the trial team in the post. We may also need to inform your GP of any abnormal blood results or relevant medical information that needs to be followed up.

Withdrawal from the trial

You are free to contact the research team to withdraw from the trial at any point without giving a reason. The investigator may also withdraw you from the trial for medical reasons, a severe adverse reaction to the treatment, or if you do not adhere to the trial schedule or complete the measures. If you lose capacity and are no longer able to consent, the Investigator will withdraw you from the trial. However if you are withdrawn from the trial we will need to use the information collected up until the time that you decided to withdraw from the trial and your anonymised data may still be shared with our research collaborators. If you discontinue the trial early, you will be asked to return to the trial centre for one final follow-up visit and undergo a number of procedures (vital signs, questionnaires, sputum, blood and urine samples and spirometry) as well as any other laboratory assessment planned at the originally scheduled follow-up visit.

Please note, the results of the Trial may be published in medical literature but you will not be named in any publications or reports about this research (it will be anonymised).

How will my samples be used?

The research team will ask for your consent to store your samples at the end of the trial in a Research Tissue Bank at the Respiratory BRC; by signing the consent form you will be agreeing to this. However, this is optional and you may opt out if you wish.

All the testing of your samples, now and in the future, will be performed for research and development purposes only. Any information derived directly



or indirectly from this research or any optional future research, as well as any patents, diagnostic tests, drugs, or biological products developed, are the property of the researchers. The results from this research and any future research may be used for commercial purposes. You will have no right to this property or to any share of the profits that may be earned directly or indirectly as a result of this or any future research. However, in signing this form and donating sample(s) for this and any future research, you do not give up any rights that you would otherwise have as a participant in such research.

Your samples will be kept in the Respiratory BRC, Research Tissue Bank for up to 25 years after the trial is completed and at that time any remaining samples will be destroyed or fully anonymised i.e. the link between you and your samples will be broken so that the samples can never be traced back to you.

If any analysis has already been performed then neither we nor our research collaborators in other academic institutions and pharmaceutical research companies are obliged to destroy the results of this research.

Can I be re-contacted for future studies?

At the end of the study you may be re-called for further tests, for which you will be asked to provide additional consent, based upon the results from this study including your genetic makeup and response (or lack of response) to treatment. This is optional and you may opt out if you wish.

Will data available the results from this study?

Environmental exposure data including local pollution and weather will be recorded by databases linked to your postcode. We shall link your data held in primary and secondary care to this study. This will enable us to understand further how the study drug works such by, for example, verifying your current treatment and to record past and future exacerbations and hospitalisations. This is optional and you may opt out if you wish.

Who is organising and funding the research?

This is a research project organised by the Respiratory BRC at Glenfield Hospital and Sponsored by the University of Leicester. The Leicester Clinical Trials Unit will be overseeing the Trial and Data Management. The results of the trial will analysed in conjunction with the Leicester Clinical Trials Unit.



The trial is being funded by Genentech. None of the doctors will be paid for including you in the trial.

Who has reviewed the trial?

All research that involves NHS patients or staff, information from NHS medical records or uses NHS premises or facilities must be approved by an NHS Research Ethics Committee before it goes ahead. This trial has been approved by East Midlands – Leicester South Research Ethics Committee. Approval does not guarantee that you will not come to any harm if you take part. However, approval means that the committee is satisfied that your rights will be respected, that any risks have been reduced to a minimum and balanced against possible benefits and that you have been given sufficient information on which to make an informed decision.

Thank you for reading this

Please keep a copy of this information sheet and your signed consent form