Participant Information Sheet

Participant Screening ID: ☐☐☐ ☐☐☐

Full Study Title	Effects of blocking TSLP on airway inflammation and the epithelial immune response to exacerbation triggers in patients with COPD. A randomized double-blind, placebo-controlled trial of Tezepelumab
Short Study Title	UPSTREAM-COPD
Sponsor	Bispebjerg Hospital, Copenhagen, Denmark
Co-ordinating Investigator	Dr Asger Sverrild, Bispebjerg Hospital, Copenhagen
Chief Investigator (UK)	Professor Chris Brightling, University Hospitals of Leicester, NHS Trust

You are being invited to take part in the above research study because you have a condition called COPD (chronic obstructive pulmonary disease). 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, please ask the nurse or doctor who gave you this sheet and they will be happy to answer any questions you may have.

1. What is the purpose of the UPSTREAM-COPD study?

COPD is characterised by chronic inflammation in the lungs which can leave you more likely to experience infections. The condition can be associated with a higher rate of morbidity and a reduced quality of life. For many years, the mainstay of COPD treatment has been inhaler medication that opens the airways. Despite this many people still suffer with exacerbations (worsening) of their COPD due to inflammation in the lungs. This can be triggered by many things, including infections. The mucous membranes in the lungs release proteins when irritated, including certain substances which lead to increased inflammation in the lungs.

The purpose of this study is to investigate the effects of a new type of medication. This medication is called tezepelumab and has been shown to help in patients with asthma. We are now trying to see if we can use the same medication in patients who have COPD. We hope that treatment with tezepelumab will reduce inflammation and airway hypersensitivity in those with COPD as well. In the UK, 20 patients will take part in this study. We are working with other research teams based in Denmark and London. Overall, between the 2 countries, 80 patients with COPD will take part in the study. Of these 80 patients, half will be given tezepelumab and half will be given a dummy drug, called a 'placebo'. We will compare the results of those two groups.

In order to understand if the treatment works, we would like to collect information from you including health questionnaires, exercise tests, breathing tests, blood, urine samples as well as collecting information from your clinical records. This study also involves two bronchoscopy

examinations of the lungs where we will take samples. This will enable us to compare information between those who are receiving tezepelumab and those who receive the placebo (dummy drug). All of these are detailed further on in this leaflet.

2. Do I have to take part?

No. Taking part in research in voluntary, and it is up to you to decide whether to take part. If you do decide to take part but change your mind later on you are able to withdraw from the study at any time without giving a reason. If you do not take part, or if you withdraw from the study, the standard of care you receive will not be affected. You do not have to decide straight away; you will be provided with adequate time to consider the information and members of the research team will be available to answer any questions you may have.

3. What will happen to me if I take part?

If you decide to take part, you will be asked to sign a consent form and you will be given a copy of this signed consent form to keep. As part of your consent, we seek permission for study personnel to view relevant sections of your medical records held by the hospital or your GP to confirm whether you are eligible to participate and to collect information about your COPD management. Your medical records will be used for the duration of the study.

4. How long would I stay in the study?

If you agree to take part, you will be asked to attend the <<insert research site>> for your study visits. At visit 1 you will be asked to sign a consent form, and after which we will ask you to complete the assessments that are listed in the visit table further on in this sheet. Once these are completed, we will check whether you are eligible to take part in the study. If you are eligible to take part in the study, you will be randomised (which is like flipping a coin) to receive either the study medication (Tezepelumab) or the placebo (dummy drug) by injection under the skin. The treatment that you receive will not be known to you or the study team and it cannot be chosen or changed. You will have an equal chance of receiving tezepelumab or the placebo. After Visit 1 you will need to return for a further seven visits at minimum over approximately 20 weeks. All visits are face to face with the research team. The table on the next page lists what will happen at each visit.

5. Study Medication

The study drug is known as ‘Tezepelumab’ and is given at a dose of 210mg subcutaneously (under the skin by injection). This is being compared to a placebo (‘dummy drug’) that will be given in the same way. Tezepelumab and the placebo are provided by AstraZeneca. Your study medication (either Tezepelumab or placebo) will be given every 4 weeks for 12 weeks. Therefore, there will be a total of 5 injections. You will be asked to come into the research unit to receive your study medication.

Once you have completed your participation in the study (or the study has finished), you will no longer receive the study medication and you will be discharged back to your GP or other healthcare provider who will determine the most appropriate medication for you at that time.

Visit Schedule
Visit 1 – Week -2 (face to face - approx. 3 hours) • Sign a consent form • Eligibility checks, medical history, health questionnaires, blood sample, height and weight, physical examination, vital signs, breathing tests, full lung function test, ECG, sputum sample, urine sample, pregnancy test (if applicable) • CT scan
Visit 2 – Week 0 (start of treatment – approx. 3 hours) • Vital signs, nasal swab • Bronchoscopy • Receive 1st dose of study medication
Visit 2.1 – Week 0 (approx. 15 mins) • Phone call follow up post bronchoscopy
Visit 3 – Week 4 (face to face - approx. 1 hour) • ECG, physical examination, vital signs, blood tests • 2nd dose of study medication
Visit 4 – Week 8 (face to face - approx. 1 hour) • ECG, physical examination, vital signs, blood tests • 3rd dose of study medication
Visit 5 – Week 12 (face to face - approx. 1 hour) • ECG, physical examination, vital signs, blood tests • 4th dose of study medication
Visit 6 – Week 16 (face to face - approx. 1 hour) • ECG, physical examination, vital signs, blood tests • 5th dose of study medication
Visit 7 – Week 20 (face to face - approx. 2 hours) • Questionnaires, physical examination, vital signs, breathing tests, full lung function test, ECG, sputum sample, blood samples, urine sample, pregnancy test (if applicable) • CT scan
Visit 8 – Week 20 (approx. 2 hours) • Vital signs, nasal swab • Bronchoscopy
Visit 8.1 – Week 20 (approx. 15 mins) • Phone call follow up post bronchoscopy

Eligibility Checks: We will check your medical records and results of any tests to check that you eligible to take part in the study.

Health Questionnaires: You will be asked to fill in questionnaires about your health, including how COPD affects you, both physically and mentally. All the questionnaires are short and each take less than 5 minutes to complete. Questionnaires will be available either on paper or via a website.

Medical History: We will ask you about your previous medical history and any current medical problems that you may have. We will ask you about medications that you are taking both prescription and over the counter to ensure it is safe for you to take part. We ask your consent for study personnel to view relevant sections of your medical records within the hospital and with your GP with regards to your clinical care for your COPD. We will only access and use information that is relevant to our research.

Physical Examination: We will listen to your heart and lungs and examine your throat. There are no risks associated with this.

Vital signs: We will measure your heart rate, breathing rate, blood pressure, oxygen levels and temperature. There are no risks associated with this.

Anthropometric Measurements: We will take your height and weight and we will use this to calculate your Body Mass Index (BMI).

Blood sample collection: You will be asked to provide blood samples to assess your health and to see how your body reacts to your allocated treatment. You will be asked to provide no more than 70ml of blood (equivalent to 4.5 tablespoons) at each visit. This may cause some mild discomfort and occasionally some bruising. At the start and end of the study, this will include a blood sample to investigate whether there are links between peoples' genetic makeup and response to COPD treatments. These tests only tell us if your genes are active ("switched on") or inactive ("switched off"). We will not be looking at your personal genetics but only observing any appreciable variation among the looks and function of different cells among patients as a group. The results do not have individual implication and there is no cut-off value to suggest as normal or abnormal. Thus, you will not be given the results of the test.

Sputum sample collection: You will be asked to provide a sputum sample. We will administer a nebuliser of salty water to help loosen it and make it easier to cough up. If this is not possible we will ask if you are able to cough up a sputum sample spontaneously.

Pregnancy test: To be eligible to participate, women of childbearing potential must have a negative urine pregnancy test at every visit where study medication is given. Both male and female participants must agree to use an acceptable method of birth control for the duration of the study. This is for safety reasons, as the effects of the study drug on an unborn baby are not known. If you or your partner become pregnant during the study, you must inform the research team immediately. We will advise you/your partner about your/their medical care and collect information about your/your partner's pregnancy and the health of the baby.

Urine sample: A urine sample will be collected to perform dipstick test.

Breathing tests: You will be asked to perform a breathing test called a Spirometry test, which involves breathing out as hard as you can several times, repeated once more after inhaling Ventolin

(salbutamol) or equivalent. You will be asked to refrain from taking your inhalers prior to these breathing tests. This will be explained fully by the study team. The breathing test may cause some temporary light-headedness and coughing. You will also be asked to perform a FeNO (fractional exhaled nitric oxide) test at the time. There are no additional risks with these.

You will also be asked to perform a test looking for specific markers in the air you are breathing out (breathprint). This will take a few minutes of normal breathing into a machine.

Full Lung Function Testing: This is a breathing test carried out with you sitting in a transparent glass cubicle with the door closed throughout the test (the door will not be locked and can be opened voluntarily at any point if required). The test measures the narrowing within your airways and the total amount of air inside your lungs. This includes the amount of air that you can breathe in and out, and the amount left inside the lungs when you have blown everything out. In front of you will be a mouthpiece to use for the test and you will be given a peg to use on your nose when instructed. This test can last between 10-30 minutes. Due to the nature of the tests and the exertion required, some people may feel dizzy, and coughing is also common.

Nasal swab: A small brush is used to take samples from the inside of the nose. This can cause mild discomfort but no other risks.

CT Scan: If you take part in this study, you will have a high-resolution Chest CT scan at visit 1. This scan may be in addition to those that you would have if you did not take part. You will also have a CT scan at visit 7. A CT scan is a type of X-ray examination that gives much more information than a normal X-ray. It produces detailed images of the lungs, breathing passages and blood vessels. The scanner itself is shaped like a large donut and is not enclosed.

These scans may be extra to those that you would have if you did not take part. This procedure uses ionising radiation to form images of your body and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure.

We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study may increase the chances of this happening to you to about 0.1%.

Bronchoscopy: A bronchoscopy is a type of endoscopic examination, allowing us to look in and take samples from within your lungs. It will involve light sedation, some medicine to open up your airways (like what you get from a blue inhaler) and some anaesthetic spray to the back of the throat. The study will involve two of these procedures, one at the start and one at the end. We will pass a scope through your nose, down the back of the throat and into the lung, where we will take some samples. In total we plan to take up to 14 tissues samples each time.

Bronchoscopy is generally a safe procedure, and it is rare to have serious complications that include bleeding, collapsed lung, cardiac arrhythmias and very rarely death. Minor but more common risks include sore nose, throat, hoarse voice, or cough after the procedure. Sometimes, you may have a

high temperature for 24 to 48 hours afterwards. Rarely, some people can develop a chest infection. There is a small risk of biopsy (taking tissue sample from your airways) as in (1 in 1000) chance of a small puncture in the lung, leading to an air leak around the lung. There is also a risk that despite the procedure we are not able to gather appropriate samples. If you have sedation, you will need someone to stay with you overnight and will not be able to drive that day. The information leaflet for further details related to bronchoscopy will be provided and a specific consent form will be requested prior to the procedure.

6. Will I be reimbursed or receive any payment for participating?

You will be reimbursed for travel and car park charges throughout the study at the usual NHS rate (45p/mile up to a maximum of £60 per visit). Please keep original receipts and bring them to each visit. We can also arrange for a taxi service should you require it. To cover any inconveniences, we will provide you with £40 for each study visit requiring additional research testing (I.e. visit 1 and visit 7), £200 for each visit requiring bronchoscopy, and £10 for visits 3, 4, 5 and 6. This inconvenience payment is on top of any travel reimbursement. Excluding expenses this adds up to £520 for participation in the whole study.

7. What are the advantages of taking part?

There are no guaranteed benefits to taking part in the study. We think that participants randomised to receive tezepelumab may have reduced symptoms and exacerbations, although this is not certain. All participants taking part in this study will be helping to make a significant contribution to research into COPD, which may improve future treatment of the condition.

Whichever treatment (tezepelumab or placebo) you receive during the study, your condition will be monitored closely to ensure you are receiving the optimal medical care. Any abnormal findings that are identified by the study procedures will be managed by the research team or reported to your GP/appropriate healthcare professional for further investigation.

8. **What are the disadvantages of taking part?**

The effects and discomforts of each individual test are outlined earlier in this leaflet. Although some of the appointments may be quite long (approximately 3 hours), we will provide refreshments and you are able to have a break whenever you need it. Following the sedation for bronchoscopy you will not be able to drive, operate heavy machinery, drink alcohol, or sign legally binding documents for 24hrs. We will not change any of your current medications unless indicated by your results. You will also be able to contact a study doctor if you have any concerns between your visits.

9. Are there any side effects of the study drug or placebo?

Tezepelumab is currently licensed for treatment of patients with asthma. Like all medications it can cause some side effects, although these are usually mild to moderate. The most common side effect is a reaction at the site of injection – such as pain, redness, and swelling, itching, or burning sensation of the skin.

There are no identified risks linked 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 study drug (this is generally a harmless salt and sugar solution). You will be monitored very carefully after each dose of your study treatment.

10. Permission to contact your GP

Your GP will be informed of your participation in this study. We may also need to inform them or other appropriate healthcare professional of any abnormal blood results or relevant information that needs to be followed up. By signing the consent form you will be agreeing that these individuals can be notified.

11. How will we use information about you?

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

This information will include your initials, NHS number, name, contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

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

We will keep all information about you safe and secure.

Some of your information will be sent outside of the UK to the study Sponsor (Bispebjerg Hospital, Copenhagen, Denmark). They must follow our rules about keeping your information safe.

If you have any research scans as part of the study then the images obtained may be used in publications or other media as part of the research study. The images will be anonymous and no one will be able to identify you from the image.

If you agree to take part in this study, your coded study data will be held in a secure database held by the study Sponsor (Bispebjerg Hospital, Copenhagen, Denmark). Furthermore, your coded study data may be shared with the Sponsor's research collaborators in other academic institutions, NHS organisations and companies involved in health and care research, for this study and for future research, in accordance with a data sharing agreement.

Once the Sponsor has finished the study, they will keep some of the data so they can check the results. An anonymised data set may be kept after the end of the study for future research. Reports will be written in a way that no-one can work out that you took part in the study.

12. 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. For example, this could be information from questionnaires, tests you have completed or results/analysis from blood tests.

We need to manage your records in specific ways for the research to be reliable. This means that we will not be able to let you see or change the data we hold about you.

13. What will happen if I do not wish to carry on with the study?

You can stop taking part in the study at any point and this will not affect the standard of care you receive. Please just let a member of the study team know.

The investigator may also withdraw you from the study. If you do withdraw, or are withdrawn, any data or samples you have already provided will be kept but no further samples will be obtained.

14. What will happen to the samples I give?

Some blood samples will be sent to the hospital laboratories to check that you are eligible to take part and to ensure your safety in taking part. Other blood samples will be taken for research to tell us more about how the study medication affects markers in your blood. We will also have samples from the breath and bronchoscopy test which we will analyse to see how the study medication affects these tissues in your lungs. Your samples will be labelled with a unique study ID number, frozen and transferred using secure containers to central laboratories both within the UK and outside of the UK to be analysed. The laboratories will follow standard procedures for handling, processing, and storage of samples. The people who will complete the tests on your samples will not be able to identify you.

At the end of the study there may be valuable samples remaining that have not been used up ('left over samples') and so, your 'left over' samples and linked research data will be stored in the Danish National Biobank (tissue bank), a structured collection of human biological material, which is accessible for future research in relation to COPD. The maximum storage duration will be 15 years. Samples and linked research data will be labelled with a unique ID (pseudonymised) and may be sent to other academic and industry collaborators for future ethically approved research. These may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Researchers using samples will not be able to identify you.

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

Further information on how data is used in research is available on the NHS Health Research Authority website, if you would like a printed copy, please ask a study team member:
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/

You can find out more about how the Sponsor (Bispebjerg Hospital in Denmark) and the University of Leicester use your information:
Email: dpo@le.ac.uk

16. What if new information becomes available?

As part of this study, we may uncover medical conditions not previously recognised. If this happens, we will assess your condition and manage your health accordingly. This may mean referring you to

other specialist teams or back to your GP for further investigations. If new safety information becomes available about tezepelumab, we will let you know and you may be asked to re-consent to the updated information.

17. What if something goes wrong?

It is very unlikely that you will be harmed by taking part in this type of research study. However, if you wish to complain or have any concerns about the way you have been approached or treated in connection with the study, you should ask to speak to the local study team on **<<insert telephone number>>** 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 the Patient Advice & Liaison Service or local complaints number on Freephone: **<<insert local PALs detail telephone number>>**; Email: **<<insert local PALs email>>**. Or they may refer you to the Sponsor's research team for further advice if this is deemed to be more appropriate.

If 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 the University of Leicester, but you may have to pay your legal costs. The normal NHS complaints service will still be available to you (if appropriate).

18. Who is organising and funding the research?

This is a research project organised by Bispebjerg Hospital in Denmark (the main trial sponsor) in collaboration with the NIHR Leicester Biomedical Research Centre – Respiratory, at Glenfield Hospital and the University of Leicester. The sponsor is the organisation responsible for ensuring that the study is carried out correctly. The study is funded by AstraZeneca. None of the study doctors will be paid for including you in the study.

19. Will I be re-contacted for future research?

With your permission, we may contact you about future research studies that you may be interested in and eligible for. This is entirely optional and agreeing to be contacted does not oblige you to take part in any future research.

If you agree, your contact details would be stored electronically on a secure server at your local research site and only authorised individuals will have access to it. You can ask us to have your contact details removed from our database at any time by contacting your local research team, or at the time you receive an invitation for future research.

20. Who has reviewed the study?

All research in the NHS is looked at 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 favourable opinion by the independent Research Ethics Committee– Yorkshire & The Hunber – Leeds East Research Ethics Committee (Ref: 23/YH/0117) and Medicines and Healthcare products Regulatory Agency (MHRA).

21. How can I get the study results?

Once the study has fully completed, a lay summary of the study outcomes will be generated for participants who are interested to receive further information.

22. What happens next?

If you would like to take part in this study, or want to discuss it further, please let someone in your care team know, or use the contact details at the end of this information sheet.

You can contact the research team on: **<<insert team contact details>>**
Principal Investigator: **<<insert local investigator>>**
Institution name: **<<insert local site>>**
Address: **<<insert address of local site>>**
Emergency contact no: **<<insert name and number>>**

Thank you for considering participation in the study and for taking time to read this information sheet.

Please keep a copy of this and your signed consent form.