PARTICIPANT information Sheet and INFORMED Consent Form

(UK)

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| NAME OF STUDY: | A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy, Safety, and Tolerability of Brensocatib Administered Once Daily for 52 Weeks in Subjects with Non-Cystic Fibrosis Bronchiectasis – The ASPEN Study |
| SHORT TITLE: | ASPEN: Randomised study to assess the effect of Brensocatib in patients with NCFBE |
| PROTOCOL NUMBER: | INS1007-301 |
| STUDY SPONSOR: | Insmed Incorporated  700 US Highway 202/206  Bridgewater, NJ 08807-1704, USA |
| STUDY DOCTOR (INVESTIGATOR): | Dr Philip Mitchelmore  Royal Devon & Exeter NHS Foundation Trust  Barrack Road  Exeter  EX2 5DW  01392 406901  Out of Hours 01392 411611 and ask for Switchboard to page the respiratory doctor on-call |
| ETHICS COMMITTEE: | Central Ethics committee – ‘London – Surrey Borders Research Ethics Committee’ |
| IRAS ID: | 1003433 |

INVITATION

You are invited to participate in an experimental clinical research study (“study”) because you have been diagnosed with non cystic fibrosis bronchiectasis (hereafter, “NCFBE”), and have a clinical history consistent with NCFBE. Joining the study is entirely up to you, before you decide we would like you to understand why the research is being done and what it would involve for you. This Informed Consent Form (“form”) describes the study to help you decide whether you want to participate in this study. It explains the purpose of the study and its details. This form describes the procedures you will be required to complete if you choose to participate in this study. It also describes potential risks and benefits of the study.

This form uses words such as treatment, drug, medication, and participant. Please remember this is an experimental study. The use of these words does not mean the drug has been shown to be safe or will improve your condition.

Some risks of this study are already known. The known risks are listed in this form to help you decide whether to participate or not. Not all potential risks are known so consider all the details carefully.

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to evaluate the efficacy, safety, and tolerability of brensocatibas treatment for NCFBE.

This is an experimental clinical research study of a study drug called brensocatib. “Experimental” means that the study drug is currently being tested in clinical research studies, and has not been approved for use in the treatment of patients with NCFBE. In addition, “experimental” means that we might not have all the information about brensocatib.

Before new drugs can be approved and sold to treat specific diseases, they must be tested in experimental clinical research studies. The results of such studies are then provided to the regulatory authorities. Brensocatib is not approved to treat NCFBE by the United States (US) Food and Drug Administration (FDA) or United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA), but it is undergoing clinical investigations to determine if brensocatib is safe and effective.

**DO I HAVE TO TAKE PART**?

No, it is up to you to decide. Your participation in this study is voluntary and you may refuse to participate or withdraw from the trial at any time without penalty or loss of benefits to which you are otherwise entitled.

The study staff will explain any words, procedures, and risks to you. You will be provided with a copy of this form to take home to read again. You may want to talk about the study with family, friends, or your regular doctor before making your decision.

If you do decide to participate in the study, you will be given this Participant Information Sheet and Informed Consent Form to sign and date, and you will be given a signed and dated copy to keep.

This study is being conducted by Insmed Incorporated (“Insmed”). Insmed is the Sponsor and is responsible for the overall cost of this study. The study doctor is being paid by Insmed to conduct the study and study-related procedures.

STUDY DESIGN

Approximately 1,620 participants between the ages of 18 and 85 years, with diagnosed NCFBE are expected to participate in this study. The study is being conducted at approximately 480 centers in North America, Europe, Japan, and the rest of the world.

If you are eligible and you choose to participate in this study, you will be randomly assigned (by chance, like flipping a coin) to 1 of the 3 study drug groups: brensocatib 10 mg tablet once per day, brensocatib 25 mg tablet once per day, or placebo (a sugar pill which contains no medicine but is in the same form as the study drug (brensocatib). The placebo looks just like brensocatib, but has no active medication in it. We do not know which study medication is the best for your condition. To try to make sure the treatment groups are the same, each participant is put into a study drug group by a computer. The study drug you get will be chosen by chance, like flipping a coin (random).

This is a double-blinded study, which means that neither you, the study doctor, nor the study team will know what study drug, brensocatib 10 mg, brensocatib 25 mg, or placebo, you have received until you complete the study. In the event of an emergency, the study doctor will be able to find out which treatment you have been given if he/she feels that knowing that information will affect your care during the emergency.

All participants will complete the same study procedures. The study will last approximately 62 weeks from the Screening (Visit 1) to the End of Study (Visit 12). There will be 12 visits including the Screening Visit (1 visit), Treatment Visits (10 visits: 6 visits are in the clinic [Visits 2, 3, 5, 7, 9 and 11], and 4 visits by telephone from your home [Visits 4, 6, 8 and 10]), and an End of Study Visit (1 visit). The End of Study Visit (Visit 12) will occur in the clinic.

You are encouraged to attend your in-clinic visits, however, if you are not able to come to the clinic due to public health concerns (for example, COVID‑19) please contact your study doctor.

Screening and Informed Consent

During your first visit, the study will be explained to you. You will have the chance to read this form and take a copy home with you to discuss with family and friends. The study staff will answer any questions you have about the study. If you choose to participate in the study, you will be asked to sign and date this form. You will get a copy of this form to keep. You must sign and date this consent form before any study procedures are performed.

After signing and dating this form, you will be evaluated for eligibility based on certain criteria:

* You will be asked some general questions about your health. For your safety, it is very important to give complete and accurate information.
* You will be asked about your medical history and any medications you are taking.

Screening tests will be performed. These tests will include:

* Questionnaires
* Medical history
* Physical examination
* Measurement of vital signs
* Pulmonary function tests
* Sputum collection
* Collection of blood and urine for laboratory testing, including a blood pregnancy test (if applicable)
* High resolution computed tomography (CT) scan of the chest if a scan has not been performed in the last 5 years, or if the available CT scan is of poor quality and cannot be read, a new high-resolution chest CT scan must be obtained.

If you are eligible and wish to participate, you will continue to the treatment period. By signing and dating the consent form you are agreeing to follow all the instructions that are provided to you by the study doctor and study staff.

STUDY DRUG AND WHAT IS EXPECTED OF YOU

The study doctor will provide the study drug and instructions for taking it. The study drug can also be delivered directly to your home by a courier if you are unable to attend a clinic visit due to a public health concern.

Brensocatib 10 mg, or brensocatib 25 mg, or matching placebo will be provided to you. The study drug is a tablet. You will be asked to take your study drug once daily before breakfast with a glass of water on an empty stomach at approximately the same time every day. It is important you take your study drug around the same time every day. On the days of in-clinic visits, study drug will be administered at the clinic by the study personnel after specific study procedures are completed. To record when you take the study drug, you will be given an electronic dosing diary. Tablets should not be broken or chewed. If a dose is forgotten but remembered before midnight of that day, the missed dose should be taken immediately. Otherwise, the dose should be skipped for that day. You will be advised to bring all your untaken tablets in the bottle in which they were provided along with your electronic diary to each visit during the Treatment Period.

The Study Doctor may interrupt the study drug dosing (ie, may stop the dosing for a period of time and then restart dosing) if, according to the Investigator’s opinion, it is in your best interest.

Follow-Up

After completing the study drug period, you will continue to be followed for 1 month while off study drug. You will be asked to stop all study drug and to return all unused study drug. A final visit will occur at Week 56 (Visit 12). This is to make sure you are in stable health before you are released from the study.

STUDY EXCLUSIONS

The study doctor will determine if you are eligible to participate in this study. Some reasons you may not be qualified include the following:

1. You have chronic obstructive pulmonary disease (COPD) or asthma
2. You receive supplemental oxygen more than 12 hours per day.
3. You have bronchiectasis due to cystic fibrosis.
4. You are a current smoker as defined per the Centers for Disease Control (CDC): an adult who has smoked 100 cigarettes in his/her lifetime and who currently smokes cigarettes.
5. There is no evidence that you have bronchiectasis (as assessed by the Bronchiectasis-Computed Tomography Scoring System).
6. You have a known or suspected immunodeficiency disorder, including history of invasive opportunistic infections (e.g., tuberculosis [TB], histoplasmosis, listeriosis, coccidioidomycosis, pneumocystosis, aspergillosis).
7. You have human immunodeficiency virus (HIV).
8. You have hepatitis B viral infection at the time of screening, or are positive for hepatitis B surface antigen (HBsAg) at the time of screening.
9. You have hepatitis C virus (HCV) infection at the time of Screening.
10. You are currently being treated for nontuberculous mycobacteria (NTM) lung infection, allergic bronchopulmonary aspergillosis, or TB.
11. You have active and current symptomatic infection by 2019 corona virus disease (COVID-19).
12. You are not able to perform an acceptable spirometry examination.
13. You are unable to follow the procedures of the study (due to language problems or psychological disorders).
14. You are receiving medications or therapy that are not allowed during the study.
15. You started oral antibiotics, or are continuing inhaled antibiotics started less than 3 months before screening that are used to treat NCFBE.
16. You are taking oral steroids (it does not matter for what reason), except steroids with topical anti-inflammatory activities (i.e., oral budesonide)
17. You have had an adjustment to your baseline medications within 1 month before Screening; however, you can be rescreened a month after the new treatment has been initiated.
18. You have an abnormal renal function test result (kidney test).
19. You have active liver disease.
20. You have a history of malignancy (cancer) in the past 5 years, except completely treated in situ carcinoma of the cervix or completely treated non-metastatic squamous or basal cell carcinoma of the skin.
21. You previously participated in a clinical trial of brensocatib.
22. You have an absolute neutrophil count <1,000/mm3 at the Screening Visit.
23. You have received any live attenuated vaccine within 4 weeks prior to the first administration of brensocatib.
24. You cough blood or coughed blood (≥300 mL or requiring blood transfusion) within 6 weeks prior to the Screening Visit or during the Screening Period.
25. You are diagnosed with periodontal disease and are either:
    1. Under active management by a dentist for this condition or
    2. Are expected to have periodontal disease-related procedures during the study.
26. You had a pulmonary exacerbation (worsening of your condition of NCFBE) 4 weeks before Screening or during the Screening period.
27. You are unable or fail to fill out the electronic diary entries (have a completion rate of less than 75%) during the Screening Period AND your compliance is unlikely to improve, according to the Investigator.
28. You have participated in any other clinical studies within 3 months before the Screening Visit.
29. You have Papillon-Lefềvre Syndrome.
30. You have other severe illness(es) that would affect your participation in the study.
31. You have abnormal laboratory values or diseases or disorders that may put you at risk by participating in the study or have a planned or anticipated major surgical procedure during the study.
32. You have a history of alcohol or drug abuse within 6 months prior to the Screening Visit.
33. Any other medical or psychological condition that, suggest a new and/or insufficiently understood disease that may interfere with study assessments.
34. You are a staff member directly involved in the conduct of the study.
35. You have a hypersensitivity (allergy) to brensocatib or to its ingredients

Your health history or screening test may show other reasons why you may not participate in the study. The study staff will discuss these with you.

**WHAT PROCEDURES ARE INVOLVED?**

You will participate in 12 visits with the study center over approximately 62 weeks. Study tests and procedures are described below:

* You will be required to attend 8 visits at the clinic (Visits 1, 2, 3, 5, 7, 9, 11, and 12)
* You will have 4 telephone calls or other virtual methods with the study doctor or staff (Visits 4, 6, 8, and 10).

You may be offered an opportunity to have some study visits performed at your home, if needed. If you and your study doctor agree to utilise home care services, a licensed nurse will contact you to schedule the visits. The home care nurses supporting this study have received specific training on this study and will communicate frequently with your study doctor and the study staff. In order to conduct the home visits, the home care nurse, the home care agency, and the home care services provider may have access to your individually identifiable protected health information, such as your name, address or telephone number. This information will only be used as necessary to schedule and conduct the home visits and will not be provided to the Sponsor of this study.

It is important that you participate in all of the visits during the study to evaluate your health and the effect of the study medicines.

You cannot eat 4 hours before each clinic visit. If you have eaten within the last 4 hours, you will be asked to come back again.

The amount of time you will spend at the clinic at each visit may vary. This is because the tests and checks will be different at each visit.

Talk to your study doctor if you want to know more about this.

You may be asked to come for extra visits, for example, if you have any side effects that the study doctor needs to look at.

Physical Health Review

At each visit, a member of the study staff will ask you about your physical health, side effects, and any medications you have taken since your last visit. For your safety, it is important to give complete and accurate information.

Physical Examination

At the Screening visit (Visit 1), and at Week 52 (Visit 11) you will have a physical examination that will include measurement of height (only at the Screening Visit) and weight (measured at the Screening Visit and at Week 52 [Visit 11]).

Additional physical examinations may be performed at any time if the study doctor feels it is necessary.

Measurement of Vital Signs

For your safety, your vital signs will be measured once at every in-clinic visit. These measurements include temperature, heart rate, respiratory rate, oxygen saturation, and blood pressure.

Electrocardiogram

An electrocardiogram (ECG) will be administered at the Screening Visit (Visit 1), and at Visits 2, 3, 7, 9, and 11. An ECG is a painless test to check the activity of the heart.

Chest Computed Tomography Scan

At the Screening Visit, you must provide a high-resolution CT scan of your chest for the study doctor to evaluate for the presence of NCFBE. If the CT scan is older than 5 years, or if the quality is such that the diagnosis of NCFBE cannot be determined from it, you will be asked to have a new high-resolution CT scan during the Screening Period (the Screening Period is up to 6 weeks long). Therefore, there is the potential of having a CT scan during the Screening Period.

CT scans use ionising radiation to form images of your body and provide your doctor with clinical information. Ionising radiation can cause cell damage that may, after many years, turn cancerous.

We are all at risk of developing cancer during our lifetime. The normal risk that this will happen is 1 in 2. This risk of taking part in this study is 1 in 2000 which is low compared to the natural risk.

Pulmonary Function Tests (PFTs)

A series of pulmonary function tests (PFTs) will be performed to see how well your lungs are working. The PFTs will be performed at the Screening Visit (Visit 1) and at Visits 2, 5, 7, 9, and 11.

Blood, Urine, and Sputum Samples

Blood samples (about 8 mL per sample or approximately one and a half teaspoons) and urine samples(about 5 mL or 1 teaspoon) will be collected at the following time points during the study: at the Screening Visit (Visit 1), and at Visits 2, 3, 5, 7, 9, 11, and 12.

During the entire study, approximately 64 mL of blood (approximately 13 teaspoons) will be collected from you. In addition, approximately 40 mL of urine will be collected (8.1 teaspoons).

Sputum samples (approximately 3 mL per sample) will be collected at the Screening Visit (Visit 1) to see if there are bacteria in your lungs.

As part of this study, samples that are not immediately used for testing can be frozen and stored. The purpose is to make these samples and information available for future research that is not yet planned. If you decide to allow storage, any part of your sample that is left over after testing will be stored for up to 2 years from the completion of the study.

If you do not wish to have your sputum samples stored for a period of up to 2 years beyond the duration of the study, you may request at any time that your samples be destroyed. The samples will be destroyed following standard laboratory procedures.

You will be informed in case of any plans for new analyses on the stored samples not mentioned above. In this case you will be asked for a new consent and you have the right to refuse any further tests.

**Smoking Status**

At each visit (both in-clinic and telephone visits), beginning with the Screening Visit (Visit 1), you will be asked about your smoking status, i.e., whether or not you smoke, how long you have smoked, whether or not you have quit smoking, and how long since quitting.

Questionnaires

During the study, you will be asked to fill out 3 electronic questionnaires. These questionnaires include the Quality of Life Questionnaire-Bronchiectasis (QOL-B) (where validated translations are available in the local language), The Bronchiectasis Exacerbation and Symptoms Tool (BEST), and the EuroQoL-5D-5L(EQ-5D-5L). You will be asked to download an app on your phone, or you will be provided with an electronic diary or other device for entering responses to the study questionnaires. This diary or device will come complete with data plan for internet access. If you decide to use a study-provided device, we ask you to look after them and you will need to return it to the study site after your participation ends. If the device has a malfunction, breaks or is stolen please contact your study site.

Where validated translations are available in the local language, the QOL-B (a quality of life questionnaire for participants with bronchiectasis) will be completed for the first time at Visit 2, and then you will complete this questionnaire every 2 weeks (up to and including Week 56) during the study using an electronic diary. If the time period for completing the QOL-B occurs at the same time as an in-clinic visit, you will wait until you are at the study site for the in-clinic visit to complete the QOL-B.

The Bronchiectasis Exacerbation and Symptoms Tool (BEST) is a daily diary for bronchiectasis symptoms that measures day-to-day changes in your symptoms. You will be asked to complete it daily on an electronic diary from the Screening Visit (Visit 1) up to Week 56 (Visit12) (in the evening).

The EuroQoL-5D-5L (EQ-5D-5L) is a 2-page questionnaire that measures mobility, self-care, usual activities, pain/discomfort, anxiety/depression, and how you feel about your health status. You will complete it on an electronic device at Visits 2, 3, 5, 7, 9, 11, and 12.

Other Assessments

Days of Work or School Missed

The study site personnel will also check to see if you have missed any work or school days due to worsening of NCFBE. This assessment will occur at every study in-clinic and telephone visit except the Screening Visit (Visit 1) and the End of Study (EOS) Visit (Visit 12).

Assessment of Pulmonary Exacerbation

The study site doctor will also check to see if you have had any worsening of NCFBE that would count as a “pulmonary exacerbation.” This means that worsening NCFBE has caused at least 3 or more of the following symptoms for at least 48 hours, and resulted in a doctor’s decision to prescribe antibiotics for you:

* Increased cough
* Increased sputum volume or change in sputum consistency
* Increased sputum purulence (for example, increased thickness and increased yellow color)
* Increased breathlessness and/or decreased exercise tolerance
* Fatigue and/or tiredness (for example, feeling of lack of healthiness)
* Haemoptysis (for example, bloody sputum)

In addition, if your doctor admitted you to the hospital or ordered intravenous (IV) antibiotics for you, these events are considered severe pulmonary exacerbation, and will be counted as such.

Assessment of Adverse Events

At every study visit beginning with Visit 2, you will be asked if you think you have had any side effects while taking the study medication. Tell the study doctor about anything that happened that caused you discomfort or concern, even if you aren’t sure it was caused by the study medication.

Dental Hygiene Education and Assessment of Oral Health

You will receive instruction on daily teeth brushing and flossing at the Screening Visit (Visit 1), and at each of Visits 2 up to 11. There is a small chance that the study drug can affect the health of your teeth and gums; however, the chance of that happening is about the same chance whether you receive brensocatib or the placebo (the placebo pill contains no active drug substance). If necessary, you may be referred to a dentist for further evaluation.

You will also undergo an examination of your teeth and gums by the study doctor each time you come to the clinic (Visits 2, 3, 5, 7, 9, 11, and 12). For each of the telephone visits, you will be asked if there are any problems with your teeth and/or gums (Visits 4, 6, 8, and 10).

Assessment of Skin Conditions

You will also undergo examination of the skin, especially of the palms of your hands and the soles of your feet, and the skin of the knees and elbows by the study doctor at Visits 2, 3, 5, 7, 9, 11, and 12 (each in-clinic visit). Brensocatib can have an effect on your skin; however, in a previous study of brensocatib, the most commonly reported skin-related side effect was “dry skin,” which was reported in 6 (3.5%) of participants who received brensocatib and 4 (4.7%) of participants who received placebo.

WHAT ARE THE POTENTIAL RISKS OR DISCOMFORTS?

Because brensocatib is an experimental drug, it is not possible to know all of the possible side effects of taking it. Some side effects may not be expected (unexpected). As with all drugs, side effects may happen.

Your study doctor will watch closely for possible health problems that may happen as a result of you taking part in the study:

* If side effects happen, they will be treated if needed.
* You may be asked to take a clinical test if you have any side effects that the study doctor needs to look at.
* The study doctor may remove you from the study if they feel this is best for you.

You must tell the study doctor or study staff about any side effects that you may have throughout the study. If you do not tell the study doctor and study staff about the side effects, you may harm yourself. To help the study doctor manage your care you should report any side effects, illnesses, or changes in your health that you notice. This is important even if you do not think these relate to the study drug.

In a previous study of brensocatib in which 170 participants received brensocatib and 85 participants received placebo, the most commonly-reported side effects (occurring in 5% or more of participants in any treatment group) were cough, headache, increased sputum, dyspnea (shortness of breath), fatigue, upper respiratory tract infection, infective exacerbation (worsening) of bronchiectasis, sinusitis (sinus infection), diarrhoea, arthralgia (pain in joints), periodontal disease, and pneumonia.

Tell the study doctor and study staff if you have any of the above symptoms, or any other side effects, during the study.

The study doctor or study staff will explain to you what to do if you start having any of the above symptoms.

Allergic Reaction Risks

There is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

* Rash
* Wheezing and difficulty breathing
* Dizziness and fainting
* Swelling around the mouth, throat or eyes
* A fast pulse
* Sweating.

If you have any of the above symptoms, contact the study doctor immediately.

You will be monitored very carefully for any signs or symptoms that you may be having an allergic reaction. Appropriate care will be taken by the study doctor and study staff if a symptom is suspected.

Are there any reproductive risks?

The effects of study drug on babies, embryos, and foetuses are unknown. It is very important that women do not become pregnant while participating in this study. All women of childbearing potential must have a negative pregnancy test before they can enter the study. A blood pregnancy test will be done at the Screening Visit. A urine pregnancy test will be performed at Baseline (Day 1) and all other visits. For telephone visits, women of childbearing potential will be provided with urine pregnancy kits; the test should be performed at home on the day of telephone visits, and results reported in the telephone visits. The study doctor may request a pregnancy test to be performed at any time during the study if the doctor decides that a test is necessary.

Women of childbearing potential must agree not to become pregnant while participating in the study. Men entering the study must agree not to make their partners pregnant. All study participants and their partners must agree to use a highly-effective method of contraception (pregnancy prevention that results in less than 1% of unintended pregnancies per year when used consistently and correctly) from Day 1 to at least 90 days after the last dose of study drug unless they are postmenopausal (no period for at least 1 year without an alternative medical cause) or surgically sterile. Women 45 years of age and younger of childbearing potential will have an additional blood test (follicle stimulating hormone or “FSH” test) to confirm fertility status at Screening. The Investigator (or a study center staff member) will explain the acceptable methods of birth control to you. You will be asked to follow their direction.

Acceptable methods of highly-effective contraception include true abstinence (refraining from heterosexual intercourse during the study), combined (oestrogen and progestogen containing) or progestogen-only hormonal contraception associated with inhibition of ovulation and supplemented with a double barrier method (preferably male condom), intrauterine devices (for example, copper IUD), intrauterine hormone-releasing systems (for example, levonorgestrel-releasing intrauterine system, progestogen implant), or vasectomized partner.

Please Note: Male participants with pregnant or non-pregnant partners (women of childbearing potential) must use condoms to avoid any chance that the study drug (brensocatib) will be passed to a developing child in the womb.

If you become pregnant, suspect you are pregnant, or your partner becomes pregnant if you’re a male participant during the study, you should notify the study doctor immediately. If you are pregnant, you will need to stop taking brensocatib immediately and will be discontinued from the study. Safety follow-up visits will then be scheduled. The outcome of the pregnancy must be reported to the Sponsor by your doctor. Additional follow-up may be required, including monitoring the health of the child for the first year after birth, if applicable. If this is the case, you will be provided with additional pregnancy related ICFs to review and sign.

If your partner becomes pregnant, she will be asked to sign and date a separate consent form to allow the study staff to collect information about the pregnancy, its outcome, and if applicable, the health of the child after birth.

Also, breastfeeding women cannot participate in this study because the study drug could pass into the body of the child with breast milk and possibly have harmful effects on the child.

Please discuss your method of contraception with the study doctor at Visit 1.

**Computer Tomography (CT) Scan**

A CT scan takes about 30 to 60 minutes. If a contrast dye is to be used for the scan, you must not drink or eat anything for 4 hours before the test, and you must remove all jewellery. A tourniquet will be applied to your arm, and a dye will be injected. You may have pain when the needle is inserted into your arm. When the contrast medium is injected during the CT scan, you may experience nausea, flushing, warmth, and/or a salty taste. You might be allergic to the contrast medium; if this is the case, please inform the study doctor.

During the test, you will lie on your back on an x-ray table. A strap will be placed across the body part to be scanned, which will prevent movement, so the x-ray picture will be clear. The table will then slide into a large, tunnel-shaped machine. You might be uncomfortable while you are in the tunnel-shaped machine. Some patients have felt claustrophobic during this test. Please speak to your doctor if you have any concerns about this. When the CT scan is finished, you may immediately resume your usual activities and diet.

CT scans use ionising radiation to form images of your body and/or provide treatment and/or provide your doctor with other clinical information. 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 that this will happen to about 50% of people at some point in their life. Taking part in this study will add only a very small chance of this happening to you.

Discomforts Caused by Study Procedures

There is no pain or discomfort during an ECG; however, removing the adhesive (sticky) pads may cause some discomfort or irritation to your skin. You may experience bruising from the blood pressure cuff.

Blood samples will be taken from a vein in your arm by using a needle. Risks that can occur with blood samples are taken include pain and/or bruising at the blood sample collection site. You may experience light-headedness or fainting at the time of the blood collection. Some bleeding, infection, or clotting at the site of the needle stick also could happen.

During the pulmonary function test (PFTs), you may become dizzy or light-headed, have chest pain, have shortness of breath, feel nervous, or feel that your heart is racing. This may be because during PFT tests, you normally have periods when you must blow out all of your air and hold your breath for a few seconds. You may feel tired when the PFT is completed. Rest until you feel comfortable before leaving the study site.

If you hold private medical or travel insurance, you may wish to check with the insurance company before agreeing to take part in this study as your taking part may affect the insurance.

POSSIBLE BENEFITS OF BEING IN THE STUDY

You may or may not benefit directly from taking part in this study. Your condition might stay the same, get better, or may even get worse while you are in this study. Your participation in this study might help doctors learn more about brensocatib as a treatment for NCFBE and help future patients.

ARE THERE ANY ALTERNATIVE METHODS OF TREATMENT?

You do not need to participate in this study to be treated for NCFBE. If you decide not to be in this study, your current treatment plan will not be affected. You can receive treatment outside of this study, if prescribed by your regular doctor.

The study doctor or your regular doctor can discuss other treatment options that are available for NCFBE and any known risks related to these treatments before you decide whether or not to participate in this research study.

By participating in this study, you are not allowed to receive treatment with the following medications, which are sometimes recommended for patients in your situation:

* Use of any immunomodulatory agents within 4 weeks before the Screening Visit (including but not limited to: bortezomib, ixazomib, thalidomide, cyclophosphamide, mycophenolate, Janus kinase inhibitors, IFN-γ, and azathioprine) is prohibited during the study up to Visit 12 (EOS)
* Continuous use of high dose non-steroidal anti-inflammatory drugs is prohibited during the study up to Visit 12 (EOS)
* Chronic use of systemic steroids for any chronic condition, except steroids with topical anti-inflammatory activities (ie, oral budesonide)
* Live attenuated vaccines are prohibited during the study (until 4 weeks after the last dose of study drug)
* Use of investigational drugs within 3 months of the Screening Visit

In addition, major elective surgical procedures and elective periodontal procedures cannot be scheduled for you while you are participating in the study.

If your regular doctor feels it is necessary for you to receive any of these treatments, you will have to stop your participation in the study.

WILL YOU BE INFORMED IF NEW INFORMATION ABOUT THE

STUDY DRUG BECOMES AVAILABLE?

While you are in the study, you will be told of any new information (good or bad) about the study drug. This new information may change your mind about being in the study. You are free to stop your participation (withdraw) in the study at any time. If you wish to stay in the study, you may be asked to sign a new Informed Consent Form to continue.

WHAT HAPPENS IF I CHANGE MY MIND?

Participation in any experimental clinical research study is voluntary.If you decide to take part in the study and later change your mind, you are free to leave the study at any time. There is no penalty if you choose not to participate or to stop participation in the study. Whether or not you choose to participate in the study will not affect where or how you receive medical care.

Even if you qualify to participate in the study at first, you may be removed from the study at any time if you, the study doctor, or Sponsor decides it is not in your best interest to continue your participation in the study. Reasons for removal include, but are not limited to, the following:

* You no longer wish to be in the study.
* You become pregnant.
* You do not follow instructions the study staff give you.
* You use a medication that is not allowed during the study.
* You no longer meet the study requirements.
* Your study doctor decides that it is the best for your safety.
* Sponsor or Regulatory Agencies decide to stop the study. Sponsor may stop this study for any reason.

If you are removed from the study before you complete all study visits, you will be asked to return for a safety follow-up visit and the study doctor will discuss the reasons for stopping the study.

If you decide to prematurely discontinue the study drug treatment, you will be asked whether you wish to continue with the remaining scheduled study visits and the follow-up.

EXPENSES AND PAYMENTS

You will not receive financial compensation or payment for taking part in this study,

You may be reimbursed for any reasonable expenses incurred as a result of taking part in this study on production of a receipt (examples include, but not limited to, meals/refreshments if your visit lasts over 3 hours, travel). Payments will either be made by your study site, or through Scout Clinical, a company working on behalf of the study sponsor to support this reimbursement process.

If the Sponsor reimburse you electronically using Scout Clinical, they will process payments for travel related expenses, stipends, and dentist/dermatologist consultations if they are needed as per protocol requirements after baseline visit. In order for Scout Clinical to support these payments, Scout Clinical will need to use certain personal information about you. This information will be collected from you by the study staff and given to Scout Clinical.

If you choose to not provide the required information or to take away consent in the future, the Sponsor will make a different method of payment available.

Scout Clinical will collect and use your information for the following purpose(s):

* ScoutPass reloadable debit card: You will be issued a ScoutPass reloadable debit card which is a debit card that your funds are loaded onto to be used at the study visits. In order to assign a ScoutPass reloadable debit card to you and load funds onto the card, Scout Clinical will need your name, address, and date of birth.
* Direct Deposit: If ScoutPass reloadable debit card is not used, Scout Clinical will directly deposit funds into your bank account. In order to transfer funds Scout Clinical will need your name, address, date of birth and bank account details.

Scout Clinical has administrative, physical, and technical safeguards that reasonably and appropriately protect the confidentiality, integrity, and availability of your personal information. Your personal information will be used and disclosed only to support the described activities, including to service providers who assist us in managing, administering or delivering the Services. Your personal information will not be shared by Scout Clinical with the Sponsor or sold, used or distributed for any other purpose. Your information will be retained for as long as necessary to provide the described activities and for compliance with applicable laws.

Your personal information will be entered into a secure website. Reasonable efforts are taken to protect the information from access by computer hackers and other unauthorised persons. All information is stored securely according to the rules and regulations provided for data storage. All your information collected on the Scout Clinical website will be deleted from the system once the study has been completed.

If your study site is participating in the PK/PD Sub-study or CT scan Sub-study, please ask your study team for a copy of the relevant ICF for details on the stipend payment for participation

The study staff will be able to answer any questions you have about the amount or availability of payments.

**WHO IS FUNDING THIS RESEARCH?**

Insmed Incorporated (a pharmaceutical company) will be organising and funding this study. Insmed will pay the hospital to cover their costs of conducting this study. If applicable, the hospital will disclose to you any financial links or other interests that they may have to Insmed.

**WHAT IF THERE IS A PROBLEM?**

You should report any study-related injury or illness to the study doctor right away. You may also call the study doctor for answers to questions about this study during the study itself.

The study doctor is independent and is not an employee or agent of the Sponsor. The Sponsor has not given the study doctor or study staff the right to make any promises or agreements on its behalf.

**Complaints**

If you have a concern about any aspect of this study, you should speak with the researchers who will do their best to answer your questions 01392 406901. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. We recommend that you obtain a copy of your hospital complaints procedure or policy if you intend to make a complaint.

**Harm**

If you are injured because of your participation in this study, you will be entitled to receive compensation in accordance with UK legislation. Please contact your study team if you feel this is the case.

Insmed will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

Insmed will pay compensation when the injury probably resulted from:

* A drug being tested or administered as part of their trial protocol
* Any test or procedure you received as part of the trial

Any payment would be without legal commitment (please ask if you wish more information on this)

Insmed would not be bound by these guidelines to pay compensation where:

* The injury resulted from a drug or procedure outside the trial protocol
* The protocol was not followed

*Copies of these guidelines are available from your study doctor on request*

**HOW WILL YOUR CONFIDENTIALITY BE RESPECTED AND THE PRIVACY OF YOUR PERSONAL INFORMATION MAINTAINED?**

The study site will record basic personal details about you, including your name, contact details, gender, height, weight and racial origin (to be used only for clinical purposes), as well as information on your medical history, and clinical data collected about your participation in the study. The following people may also access these records:

* Study monitors and auditors, who may work for Insmed Incorporated or its authorised agents, who check that the study is being performed correctly and that the information collected about you is accurate;
* Ethical committee that approved this study and ensures that your rights and well-being are safeguarded;
* National and international regulatory authorities involved in keeping research safe for participants;
* Clinical trial recruitment company if you were referred to the study by such a company, for analytical purposes and so they may be compensated.

To ensure privacy, your name and other directly identifying information will not be attached to records or samples released to Insmed Incorporated and its service providers for research purposes. Instead, you will only be identified by a code. Only the study doctor and authorised personnel will be able to connect this code to your name, by a list that will be kept securely by the study site for 15 years. Your date of birth and initials may also be recorded to help identify your study record. Your coded data will be forwarded to Insmed and its service providers for activities related to the study e.g. laboratory analysis. A list of companies to whom your coded information is transferred is available from Insmed via your study doctor.

Under the Data Protection Act 2018, Insmed Incorporated makes important decisions on how your information collected for the research project are used and disclosed and is responsible as ‘controller’ for ensuring that the rules of this law are followed. The study site will have similar responsibility in respect to the handling of data in your medical files at site. To the extent there is no conflict with the purpose of the study, you have the right to access, through your study doctor, all the information collected about you and, if applicable, ask for corrections. You may have the additional rights to object to how your information is being handled, request deletion of your data, restrict aspects of the processing of your information or ask for a copy of your data to be provided to you, or a third party, in a digital format. Note however, in order to protect the scientific integrity of the study, the treatment you receive in this study needs to remain unknown (= blinded) until the study data is analysed.   
  
You also have the right to complain about how your information is handled to a supervisory authority that is responsible for enforcing data protection law. In the UK, this is the Office of the Information Commissioner.

Recipients of your information may be in countries that do not provide the same standard of legal protection for your information as in the United Kingdom, raising the risk that you will not be able to enforce the above rights and recipient organisations may not be legally required to fully secure your data. Certain international recipients of your information may have signed special contracts to provide legal protection for your transferred information (e.g. so called “Standard Data Protection Clauses”). In any event, all parties involved in the study are required to maintain your confidentiality.

Your information is collected, used and disclosed in the interest of Insmed Incorporated conducting scientific research. You are asked to consent to various uses and disclosures of your information at the end of this form.

If you should withdraw from the study, data collected prior to your withdrawal may still be processed along with other data collected as part of the study. Normally no new information will be collected for the study database unless you specifically consent to that. However, the law does require that any side-effects you may suffer are documented. You have the right to require that any previously retained samples are destroyed.

This study may only be performed by collecting and using personal information on study participants as described in this form, therefore you may only participate in the study if you agree to the collection and use of your information as described here.

If you have any questions, comments or complaints about how your information is handled in this study, or wish to obtain a copy of the Standard Data Protection Clauses, you should firstly contact your study doctor who will be able to direct your query where appropriate to staff responsible for data protection at Insmed or site, including the site Data Protection Officer.

**WHAT WILL HAPPEN TO ANY SAMPLES I GIVE?**

The blood and urine samples collected during the study will be used for routine tests and analysed at a central laboratory PPD Laboratories EU, Clusterpark, Kleine Kloosterstraat 19, 1932 Zaventem, Belgium. Additionally, blood and urine samples will be stored for a period of up to 2 weeks (and sputum samples for up to 2 years) before discarding after test date, unless otherwise required by the institution participating in the study. The samples will be stored at central laboratories and only be accessible to authorised laboratory personnel and Insmed.

The sputum samples collected during the study will be used to test for bacteria causing your infection and will be sent to International Health Medical Associate (IHMA) EU, Rte. de I'Ile-au-Bois 1A, Monthey/VS, 1870, Switzerland for analysis. The sputum samples will be stored for up to 24 months.

If you do not wish to have your sputum samples stored for a period of up to 2 years beyond the duration of the study, you may request at any time that your samples be destroyed. The samples will be destroyed following standard laboratory procedures.

To ensure privacy, your name, initials and other directly identifying information will not be attached to records or samples released to Insmed Inc. and its service providers for research purposes. Instead, you will only be identified by a code.

You will be informed in case of any plans for new analyses on the stored samples not mentioned above. In this case you will be asked for a new consent and you have the right to refuse any further tests.

**HAS THE STUDY RECEIVED MEDICAL OR ETHICAL APPROVAL?**

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 the Central Ethics committee – ‘London – Surrey Borders Research Ethics Committee’.

**INVOLVEMENT OF THE GENERAL PRACTITIONER/FAMILY DOCTOR (GP)**

Your General Practitioner (GP) of family doctor will be notified of your involvement in this study. They will be asked to pass relevant information about your health status and medication changes to the study doctor.

WHO CAN YOU CONTACT WITH FURTHER QUESTIONS?

You may ask questions about this information sheet and consent form at any time.

* For study-related questions, contact the study Sponsor or study staff at the telephone number(s) listed on page one of this form.
* For study-related injuries or emergencies, contact the study Sponsor or study staff at the telephone number(s) listed on page one of this form.
* For more information about your rights as a research participant or complaints about the study please direct enquiries to: PALS (Patient Advice and Liaison Service) at the Royal Devon and Exeter Hospital on telephone number: 01392402093 or email: rdetr.pals@nhs.net.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>. At most, the Website will include a summary of the results. You can search this website at any time.

Do not sign this consent form unless you have had the chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to participate in this study, you will receive a signed and dated copy of this information sheet and consent form for your records. Thank you for taking the time to read this information.

**Participant Consent UK**

|  |  |
| --- | --- |
| **Principal Investigator:** | Dr Philip Mitchelmore |
|  |  |
| **Participant initials:** |  |
| **Participant number:**  **Short Title:** | ASPEN: Randomised study to assess the effect of Brensocatib in patients with NCFBE |

|  |  |
| --- | --- |
| **Statement of Consent** | ***Please initial box*** |
| I have read (or someone has read to me) the information provided above. I confirm that I have had ample time to read (or have read to me) and understand the information for this experimental clinical research study (“study”). I have been given a chance to ask questions to help me understand what my participation in the study will involve. All my questions have been answered to my satisfaction. |  |
| The study staff gave me information about what will happen during this study. I was told how long this study will take. I was told how this research may affect me or my health. This information included possible inconveniences, discomforts, or risks of this study to me. |  |
| I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my medical care or legal rights being affected. |  |
| I confirm that I have told study staff about any clinical research study that I am participating in or have participated in within 3 months before the Screening Visit. |  |
| I understand that the study doctor or Sponsor may end my participation in this study at any time, for any reason, and without my agreement. The reasons for doing so will be explained unless the reason becomes known after the study visit has ended. |  |
| **What will happen to your data?**  By signing this form you provide consent for your information to be collected, used and shared as described:   * The authorised representatives of Insmed Incorporated, the Ethics Committee and regulatory authorities’ inspectors may have direct access to your medical records. * Study data, including your coded medical information, may be retained and later used for further research into your medical indication, unless you object. * Study data may be transferred to other countries for study purposes, including countries not providing the same standard of legal protection for your personal information as in the European Union. |  |
| I give permission for personal information to be shared with Scout Clinical (third party) as outlined in the ‘Expenses and Payments’ section of this information sheet.  Yes 🞏 No 🞎 |  |
| I agree to my GP being informed of my participation in the study as described in this information sheet |  |
| I specifically agree to my personal information and blood samples collected during the study being sent outside the European Union as described in this information sheet |  |
| I understand that I will receive a copy of this signed and dated information sheet and consent form |  |
| By signing this form, I have not given up any legal rights that I would otherwise have as a participant in an experimental clinical research study. |  |
| If due to Covid-19 I cannot attend a site visit, I understand that my name, address, and other personal information may be provided to service providers who are responsible for providing me services related to home health care, and drug delivery.  Yes 🞏 No 🞎 |  |
| I voluntarily agree to take part in this study |  |
| Optional Future use of Samples  I agree to the storage of my unused samples for future research use.  Yes 🞎 No 🞎 |  |

**Participant Consent UK**

|  |  |
| --- | --- |
| **Principal Investigator:** | Dr Philip Mitchelmore |
|  |  |
| **Participant initials:** |  |
| **Participant number:**  **Short Title:** | ASPEN: Randomised study to assess the effect of Brensocatib in patients with NCFBE |

**Participant**

Printed Name Signature Date Time (24 Hr)

**Witness (if applicable)**

Printed Name Signature Date Time (24 Hr)

* I have presented the study and answered the participant’s questions
* I will give the participant a copy of this signed and dated Informed Consent

**Presenter (Investigator or Delegate)**

Printed Name Signature Date Time (24 Hr)

*when complete: 1 for participant, 1 for researcher site file; 1 to be kept in medical notes*