

Subject Consent/Assent Form Template - FinalProtocol CP-AI-005

**SUBJECT CONSENT/ASSENT AND PERMISSION BY PARENTS AND  
GUARDIANS FORM**

**PROTOCOL CP-AI-005**

**A Phase 3, Double-Blind, Multicenter, Randomized, Placebo-Controlled Trial with  
Aztreonam Lysinate for Inhalation in Cystic Fibrosis Patients with Pulmonary  
*P. aeruginosa* Requiring Frequent Antibiotics (AIR-CF2)**

**Investigator (research doctor):**

**Institution name:**

**Institution address:**

**24-hour emergency telephone number: (###) ###-####**

**Approved by Institutional Review Board:**

**Patient Number:** \_\_\_\_\_

**Patient Initials:** \_\_\_\_\_

*Parent(s) and legally authorized representative(s) (guardian(s)) signing on behalf of the child should refer to "your child" when reading "you".*

**Your Rights as a Study Participant**

You are being asked to be part of a research study. This consent form tells you details you should know about the study. Your study doctor or nurse will go over this consent form with you and answer any questions you may have. The most important issue for you to understand is that no one can force you to take part in this study. Even if you agree to participate now, you are free to change your mind and stop at a later time without any penalty or loss of benefits to which you would otherwise be entitled.

This form may contain words that you do not understand. Please ask the study doctor or other staff to explain anything that you do not clearly understand. You may also ask questions about the purpose of the research, what you will be asked to do, the possible risks

and benefits, your rights as a volunteer, and anything else about the research or this form that is unclear. When all your questions have been answered, you can decide whether you want to be in the study. If you agree to take part, you will be required to sign this document to show that you have reviewed the contents, have had your questions answered, and are choosing to be in the study.

**Why is this study being done?**

You are being asked to volunteer in this study because you have cystic fibrosis (CF). The purpose of this research study is to test an experimental drug called aztreonam lysinate for inhalation (AI, study drug).

People with CF often have lung infections that occur repeatedly or worsen over time. The lung infections are caused by bacteria (germs). Treatment with antibiotics (a type of medicine) is used to stop or slow down the growth of the bacteria. The antibiotics may be given by mouth, into a vein (IV) or inhaled as a mist. Research has shown that inhaling an antibiotic as a mist is an effective way to treat lung infections in CF.

A study of AI in 105 CF patients aged 13 years and older with the same lung infection you have has just finished. No serious side effects related to the AI study drug were reported during the study.

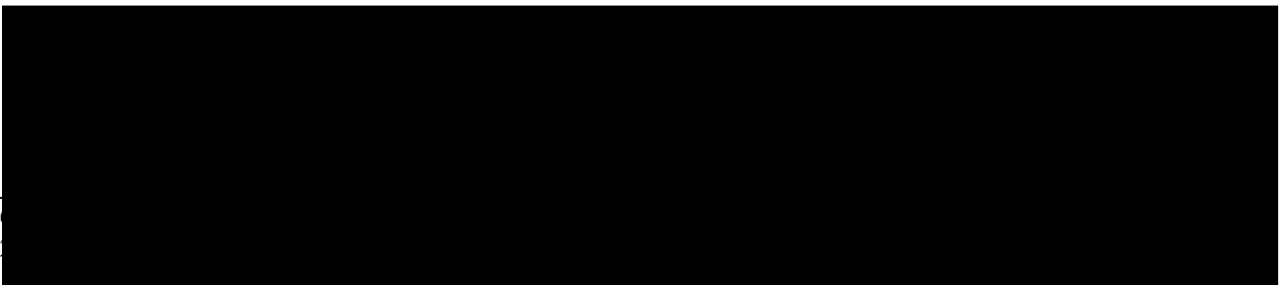
The purpose of this study you are being asked to take part in is to find out if AI is safe and effective in CF patients with lung infections. AI is an investigational drug. The US Food and Drug Administration (FDA) is allowing it to be used in people for clinical research purposes only.

**Who will participate in this study?**

About two-hundred and fifty (250) males and females six years of age and older from about 50 study centers in the United States will be participating in this study.

**What will you have to do if you decide to participate in this study (study procedures)?**

If you decide that you want to take part in this study, you will be in the study for up to 126 days and will return to the clinic for 9 study visits. If you meet all study requirements, you will first receive a 28-day course of tobramycin solution for inhalation (TSI) (TOBI®)



treatment to be taken as you normally do at home. An LC PLUS<sup>®</sup> nebulizer will also be given to you. After you finish your course of TSI, you will be randomized to receive treatment with either 75 mg AI (active drug) twice or three times daily or placebo (sugar powder containing no drug) twice or three times daily. This is done by chance, like flipping a coin. You will have two times the chance of getting active AI drug than you have receiving placebo.


Everyone will receive TSI. Treatment with AI or placebo will be blinded, meaning, you, your study doctor, and the sponsor of this study, [REDACTED] will not know whether you are taking AI or placebo during the 28-day treatment period. The information about whether you are receiving AI or placebo will be made available to your study doctor in the case of an emergency.

AI or placebo will be taken by using the eFlow electronic nebulizer<sup>®</sup>. The eFlow is a reusable device that mixes air with the study drug solution (AI or placebo) so that it becomes a mist you inhale as you breathe. The device works using a vibrating membrane (thin metal layer with many holes) that helps deliver AI or placebo to your lungs within minutes, minimizing the amount of drug left in your mouth and throat. The eFlow is permitted for use by the FDA.

**The following describes what will occur at each study visit:**

You will be required to take a short acting bronchodilator, a medicine to open your airways, before receiving a dose of AI or placebo study drug. You will also be given instruction when to use the bronchodilator at home.

**Visit 1, Screening:** The screening visit lets the doctor know if you are able to participate in the study. The study doctor will explain the study to you. If you think you want to be in the study, you and your parent(s)/guardian(s) (if applicable) will be asked to sign this consent form. Your doctor will then do the following to see if you are a match for the study:

- 1) Ask you questions about your medical history.
  - 2) Perform a physical exam including vital signs (temperature, heart rate, breathing rate and blood pressure).
  - 3) Measure your height and weight.
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- 4) Perform spirometry (PFTs) – you will blow into a machine to check your lung function (you will receive an inhaled medicine [bronchodilator] to open up your airways before the spirometry).
- 5) Collect a small amount of blood (2 to 3 teaspoons) to check your blood count, and liver and kidney function. Females of childbearing years will also have a pregnancy test performed.
- 6) Perform a chest X-ray – only if you have not had one within the previous 90 days prior to screening or have had a significant illness since your last chest X-ray.
- 7) Perform oximetry – a small clip will be placed on your finger to measure the amount of oxygen in your blood.
- 8) Collect some sputum – at least 1 gram (two tenths of a teaspoon) will be collected to test for current lung infections.

This screening exam will take approximately 2 to 3 hours to complete.

If you decide to participate and your doctor feels that you are still a match for the study, you will be asked to come back to the clinic to start the study within 7 to 21 days for Visit 2.

When you return for Visit 2, you will have some tests and procedures done by your doctor (like those done at Visit 1) to make sure that you are still eligible to participate in the study. If you are still a match for the study, you will be given a 28-day course of TSI. You will take your first dose at the clinic and then take the rest at home. After you finish your course of TSI, you will return to the clinic for more tests and procedures (Visit 3). If you come to the clinic before you finish all your TSI treatment, you should take your last dose of TSI the day before your visit.

At Visit 3, you will take your first dose of AI or placebo at the clinic. After your tests and procedures, you will receive a 28-day course of either AI or placebo to take at home twice or three times a day. Your doctor will tell you how many doses you will need to take. You will then return to the clinic every two weeks for the next 12 weeks to have tests and procedures conducted.

The following is a list of tests and procedures that will be done at some or all of your clinic visits.

1. **Current Medications and Adverse Events:** Your doctor will review any current medications you are taking and ask you how you have been feeling.

2. **Physical Examination:** Your doctor will perform a physical examination that will include taking your height and weight. Your blood pressure and heart rate will also be assessed. In addition, your doctor will see if you need to take medication for your CF symptoms. If you do need to take an IV or inhaled antibiotic, you will receive your treatment but will discontinue the study.
3. **Missed School/Work Days:** Your doctor will ask you how many days of school or work that you missed because of your CF symptoms since your last visit.
4. **Blood Collection:** At Visits 1, 3, 4, 5, and 6, a small amount of blood (2 to 3 teaspoons) will be collected from a vein in your arm to check your blood count, liver and kidney function, and immune response. At Visits 3, 4, and 5, a little more blood will be collected to see how much AI drug is in your body.
5. **Sputum Collection:** Some of your sputum will be collected at Visits 1 to 7 so we can assess how active your infection is. A little more sputum will also be collected at Visits 3 and 4 to see how much study drug is still in your system.
6. **Bronchodilator (BD):** All patients will take a short acting BD within 60 minutes of taking AI or placebo. Patients will only take a BD before taking TSI if normally prescribed by the doctor. All patients will take a short acting BD before spirometry is performed at all clinic visits.
7. **Spirometry (PFTs):** You will blow into a machine to check your lung function. You will also take a dose of a short acting bronchodilator before blowing into the machine. At Visits 2, 3, and 4, you will have spirometry performed both before and after you take a dose of TSI (Visit 2) and AI/Placebo.
8. **TSI and AI/placebo taken at the clinic:** At Visits 2, 3, and 4, you will take TSI (Visit 2) and AI/placebo (Visits 3 and 4) at the clinic. At these visits, you will have some tests done both before and after you receive your treatment. If you return to clinic at Visit 3 before you use up all your TSI, you should be sure to take your last dose of TSI the day before the visit.

When you return for Visit 4, be sure your last dose of AI or placebo was taken at least 4 hours before your clinic visit.

**You need to remember to bring one dose of AI/placebo and your eFlow to the clinic at Visit 4.**

9. **TSI & LC PLUS and AI/placebo & eFLOW Dispensed/Return:** At Visit 2, you will be dispensed TSI and an LC PLUS which you will take at home for 28 days. At Visit 3, you will return all used and unused TSI to the clinic. After your tests and procedures at Visit 3, you will be given a 28-day supply of AI/placebo and the eFLOW nebulizer. You will return all used and unused AI/placebo at Visit 5.

10. **Questionnaire Completion:** You will complete the quality of life **Cystic Fibrosis Questionnaire (CFQ-R)** and the **Patient's Global Rating of Change Questionnaire**. These forms ask a number of questions about how you are feeling. Your doctor or study nurse will show you how to complete this form, but you will need to complete this by yourself. Your answers to both of these questionnaires will not be given to anyone, including your parents/guardian (if applicable).

The Cystic Fibrosis Questionnaire (CFQ-R) helps us better understand how CF affects your daily activities and how much you may benefit from the study drug. The Global Rating of Change Questionnaire will help us assess these changes.

If you are between 6 and 11 years old, you will have the questionnaires given to you by either the study doctor or the study nurse.

If you are 12 years old or older, you will complete the questionnaires on your own.

For children and adolescents between 6 and 13 years old, a parent/guardian will also be asked to complete two parent/guardian questionnaires. The same parent/guardian will need to complete these questionnaires throughout the study. If the same parent/guardian is not able to make it to one of the visits, please inform the study doctor or nurse before the visit to discuss whether or not the questionnaires can be completed at that visit.

The CFQ-R will be completed at Visits 1, 2, 3, 4, and 7. The Patient's Global Rating of Change Questionnaire will be completed at Visits 2, 3, 4, and 7.

**Sputum Storage**

A little bit of sputum you give at study visits will be stored for possible future microbiology testing to see whether your bacterial infection(s) has developed the ability to block the action of the study drug (drug resistance testing) and for other exploratory analyses. These storage samples will be collected at all routine visits during the study up to Visit 7.

**Are there any procedures in this study that are not usually part of my routine doctor examinations (experimental procedures)?**

The AI study medication is an experimental treatment. The use of a placebo (sugar powder containing no drug), the blinding to what study treatment you will receive (you, your doctor and the Sponsor will not know what treatment you receive), and the blinded treatment randomization (study drug selection by chance) are procedures done only for research studies. Sputum and blood sampling for aztreonam (the antibiotic) levels are only being done for the purposes of the study and may not be part of your routine care.

The questionnaires involved in this study are not routine parts of your care. The questionnaires will take about 20 minutes to complete.

**Is there anything I should or should not do while I am in the study (study rules)?**

If you decide to be in this study, there are certain rules you must follow before, during, and after the study period. Some are listed below, but there could be others that your doctor will discuss with you.

- 1) You must not become pregnant during this study.
- 2) It is very important that you tell your doctor all the information you know about your health and any medications you may be taking throughout the study period. If you do not tell the study doctor everything you know, you may be putting your health at risk.
- 3) You must return all of the used and unused TSI and AI/placebo to the clinic. At Visit 3 you will return TSI and at Visit 5 you will return AI/placebo. You must also return the eFlow to the clinic at Visit 5. When you are home, you should remember to track any doses of medication you miss and tell your study doctor or coordinator at your next visit.

- 4) You must follow all rules and procedures given to you while you are participating in the study. If you do not, you will be discontinued from the study. If you are unsure about what you are supposed to do, you must ask the research doctor or coordinator to explain it to you.

**What are the risks of participating in this study? Will any of the procedures cause any discomforts?**

**Risks of AI/Placebo Blinded Study Treatment**

It is possible for any drug to cause unwanted side effects. You need to know about side effects that could occur in this study before you agree to participate.

As with any inhaled drug, taking AI or placebo may cause irritation of the airways. Side effects associated with AI include increased cough, shortness of breath, wheezing, chest tightness, unpleasant taste, and decrease in lung function. Bronchoconstriction (narrowing of the airways) is a potential complication associated with any inhaled medication.

Other possible side effects may include diarrhea, bloating, stomach pain, nausea, and vomiting.

Allergic reactions can also occur with any drug. Common symptoms may include rash, itching, or skin problems.

**Risks of TSI (TOBI®) Treatment**

TSI is an FDA approved medicine. The most commonly reported respiratory side effects associated with TSI include increased cough, pharyngitis (sore throat), increased sputum, feeling weak, rhinitis (inflammation of the nose), and difficulty breathing. Other non-respiratory side effects associated with TSI include tinnitus (ringing in the ears) and voice alterations (changing). Please see the TSI package insert if you want more information related to TOBI treatment.

**Possible Risks/Discomforts of Study Procedures**

**Blood Draws:** The blood draws taken during this study may cause discomfort. You may feel a sting when the needle is put in your arm to take blood. It is possible that there may be

some swelling, bleeding or bruising where the needle enters the skin. Some people have also felt light-headed when their blood was being taken. About 2 to 3 teaspoons will be collected at each blood draw.

**Spirometry:** You may have some coughing or shortness of breath after spirometry, but there is no pain expected to be associated directly with these tests.

**Chest X-ray:** A chest X-ray (or chest radiography) provides your doctor with an image of your heart, lungs, and surrounding organs. Getting an X-ray is like having a picture taken; the procedure should not cause any pain. Because the X-ray procedure involves the use of radiation, there is a very low risk from radiation exposure. However, there are procedures in place to make sure that the least amount of radiation is used. Pregnant women and children are most susceptible to the risks of radiation exposure.

**Are there any unknown risks of participating in this study?**

All of the tests and measurements performed during this study are designed to watch you closely for any signs of side effects to AI. AI is still being tested for the treatment of CF; therefore, it is possible that there may be other side effects that we do not know yet. If any new information about the study drug is known during this study, the study doctor will immediately tell you or your parent(s)/guardian(s) so you can decide if you still want to be in the study.

**Pregnancy and Birth Control**

The effects of AI on an unborn child are not known at this time. Therefore, if you are sexually active, you must use adequate birth control measures while participating in this study. Acceptable methods include birth control pills, Depo-Provera, diaphragm, intrauterine device (IUD), cervical cap, abstinence, or condom with sponge/foam. All women who can become pregnant must have a negative pregnancy test prior to starting treatment with study drug. If you become pregnant during this study, you must stop taking the study drug and call your doctor immediately.

**Are there any benefits of my participating in this study?**

You may have some improvement in your health (benefit) from the study medication (AI) you receive in this study. However, it is possible that the medication will not produce any benefits or that the benefits may only be temporary. The main goal of this research is to learn more about how AI can help patients with cystic fibrosis. The results of this study could also help in the future to treat other patients like you who have cystic fibrosis.

**Will I receive any payment or compensation for participating in this study?**

It will not cost you any money to participate in this study. You will receive a small payment for participating in this study to cover food and travel to and from the clinic (\$50 per visit for Visits 1, 5, 6, 7, 8, and 9; \$75 per visit for Visits 2, 3, and 4). All clinic visits, laboratory testing, TSI treatment, the LC PLUS for TSI administration, study drug (AI/placebo) and the eFlow for study drug (AI) administration you will receive are free.

**Who is organizing and funding this study?**

This study is organized by [REDACTED] who will pay the study doctor or his/her institution for the work he/she does if you are included in this study. [REDACTED]

[REDACTED] has also provided some funding to [REDACTED] for this study

**Are there any alternative treatments if I don't participate in this study?**

An alternative to taking part in this study is to continue with your current treatment for CF. CF treatments may include use of other antibiotics, such as TSI, to treat infection. You may choose not to participate in this study and keep taking your current treatment, or you may choose not to receive any treatment at this time. If any new therapy becomes available for CF, your doctor will tell you.

**Your participation in this study is voluntary and completely up to you.**

**What if new information becomes available?**

Your doctor will tell you and/or your parent(s)/guardian(s) about any significant new information that becomes available during the study that may affect your willingness to continue the trial. You should discuss this with your study doctor.

**What if I change my mind and no longer want to participate in the study?**

**Participation in this study is voluntary and it is entirely your choice to be in the study or not. You do not have to be in this study and no one will be mad or treat you differently if you choose not to.**

If you do choose to be in the study, you may change your mind at any time and stop the study. Your decision not to take part in this study or to stop your participation will not affect your medical care or any benefits to which you are entitled. If you no longer want to participate in this study, you should tell the study doctor or study staff immediately. You will be asked to return for a final study visit so the study doctor can perform safety tests (physical exam, heart rate and blood pressure measurements, spirometry, blood sampling) and to return all used and unused study drug supplies and the device.

It is also possible that the study doctor or your regular doctor may decide that you should be taken out of the study. This could happen because it is no longer safe for you to continue in the study or if you are not following rules or instructions given to you by the study staff. The study sponsor who is running this study may also decide to take you out of the study or end the study at any time.

**What happens if I get sick during the study?**

If you get hurt or sick as a result of being in this study, the study sponsor will pay for any medical care you might need that is not paid for by your insurance. This assistance will be provided as long as you followed all study-related instructions given to you by your study doctor or study staff, and you told the study doctor of your injury or illness as soon as it happened. This treatment will include any necessary emergency treatment and proper follow-up care. Injuries caused by the negligence of any person, or the intentional misconduct of any person outside of [REDACTED] will not be covered by [REDACTED]

[REDACTED] No other compensation for such injury is available.

The sponsor will not pay for things like lost wages, disability (payment while you are not able to work because of an injury), or discomfort due to injury or illness. By signing this consent form you do not give up any of the legal rights you have as a participant in a research

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study in the event of negligence (carelessness) or other legal faults of anyone involved in the study.

You should notify your study doctor of your injury or illness immediately. The doctor's phone number is located on the front page of this form.

**Confidentiality**

Information collected for this study is confidential. Data collected from you and other participants in this study will be shared with other doctors in the research field, but no names of patients will be used. There will be no names or other patient identification in any study documents. Your records may also be reviewed by representatives from regulatory authorities (including the US Food and Drug Administration (FDA)), the Institutional Review Board (IRB), and [REDACTED]. If your study record is reviewed by any of these groups, they may also need to review your medical record. Data collected and recorded on study forms are the property of [REDACTED]. In the event of any publication regarding this study, your name will not be disclosed.

**Who can I contact if I have questions about the study?**

You may ask the study doctor and study staff any questions you may have about this study at any time. If, at any time during this study, you or our parent(s)/guardian(s) have any questions about the study or would like additional information about the study drug (AI), please contact \_\_\_\_\_, at (###) ###-####.

If you think you have experienced an injury due to being in this study or if you do not feel well at any time during the study, you should call Dr. \_\_\_\_\_, at (###) ###-####.

If you have any questions about what it means to be part of a research study, you can call the people at the Institutional Review Board (the committee that approved this research project) at (###) ###-####.

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**VOLUNTEER'S STATEMENT**

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about taking part in this study or about a research-related injury, I may contact \_\_\_\_\_ at \_\_\_\_\_.

I understand that my participation in this research project is voluntary. I know that I may quit the study at any time without affecting my future medical care or losing any benefits to which I might be otherwise entitled. I also understand that the research doctor or person(s) in charge of this study may decide at any time that I should no longer participate in this study.

If I have any questions about my rights as a research subject in this study I may contact:

**IRB Chairperson Name**

**Address**

**Telephone (collect calls will be accepted)**

By signing and dating this consent form, I have not waived any of my legal rights or released the parties involved in this study from liability for negligence.

I have read and understand the above information. I agree to participate in this study. I have been given a copy of this signed and dated form for my own records.

\_\_\_\_\_  
Signature of participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of participant

\_\_\_\_\_  
Signature of legally authorized representative

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of legally authorized representative

\_\_\_\_\_  
Name and Title of person who explained the study

\_\_\_\_\_  
Signature of person who explained the study

\_\_\_\_\_  
Date