NATIONAL JEWISH HEALTH
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM FOR RESEARCH WITH HUMAN SUBJECTS

Protocol Title: IV Colistin for Pulmonary Exacerbations: Improving Safety and Efficacy

Principal Investigator: Milene Saavedra, M.D.

Phone number: 303-270-2333

Introduction

You are being invited to participate in a research study. Research studies include only people who choose to take part. Please take your time making a decision. Feel free to discuss it with your friends, family, and doctors. Before agreeing to take part in this research study, it is important that you read this consent and authorization form because it describes the study and any of the risks that it may involve. No guarantees or promises can be made regarding your experience in the study. Please ask the study doctor or the study staff to explain any words, ideas, or information not clear to you.

Why is this study being done?

You are being invited to take part in a research study. The purpose of this study is to find the safest and most effective way to administer IV antibiotics to treat acute pulmonary exacerbations (APEs) in patients with cystic fibrosis (CF) that are caused by pathogens, like *Pseudomonas aeruginosa*. This study will test the safety and effectiveness of two commonly prescribed IV antibiotics: tobramycin and colistin. Though regularly used, not much is known about how these drugs compare with each other in terms of their toxicities, both during short term treatment of an APE and after many treatment courses with these drugs over many years. There are currently no guidelines on the safest and most effective antibiotics to use when treating APEs.

We will study kidney function, sputum cultures, and treatment outcomes in patients receiving routine administration of one of these two IV antibiotics. We will also test these outcomes in patients receiving a less frequent dosing schedule for IV colistin. The hope is that this new schedule for IV colistin, which is twice a day and adjusted based on blood and urine tests, will reduce harmful side effects, such as kidney damage, while still being a powerful treatment against CF microbial pathogens.

Subject's Initials: _____

You are being asked to participate in this study because you have CF and are 18 years of age or older. You have been diagnosed with an APE by your CF physician and will be starting either IV tobramycin or IV colistin.

How many people will be in this study?

Up to 90 people will be enrolled in this study at National Jewish Health │ Saint Joseph Hospital. This study will last for 3 years.

What will happen if I enroll in this study?

Once your CF physician has determined you will be starting on IV antibiotics, you will be randomized into one of three treatments:

- IV tobramycin administered once a day, as per standard dosing schedules.
- IV colistin administered three times a day, as per standard dosing schedules.
- IV colistin administered twice a day and adjusted based on how your body is able to absorb, or take up, the drug.

Randomization means that you are put into a group by chance. Neither you nor the researcher will choose what group you will be in. You will have a one-in-three chance of being placed in any group. If your physician thinks it is unsafe for you to be treated with tobramycin, you will be randomized into one of the two IV colistin treatments.

If you decide to enroll in this study, your participation will last for 14 days while you are receiving IV antibiotics in the hospital. If you leave the hospital before 14 days, you will still remain in the study and we will use the data already collected.

The following procedures may take place while you are in the study. Some of these procedures are for research purposes. Some of them are part of your clinical care.

- **Sputum collection** – we will ask you to try to cough up some mucus (sputum) so we can measure the levels of antibiotics in your sputum. This is for research.

- **Blood collection** - up to 10mls, or 2 teaspoons, will be collected to measure the levels of antibiotics in your blood. This will be done twice during your hospitalization. The blood can be drawn by putting a needle into your vein or through your PICC line or a Medi-port, if you have one. This is for research.

- **Urine collection** – you will be asked to collect urine at each study visit. We will use this to measure the levels of antibiotics in your urine. If you have an abnormal blood test (high serum creatinine), your urine will also be tested for kidney damage. This is for research.

- **CF Health Related Quality of Life questionnaire (CFQR):** this questionnaire asks questions about your symptoms and how they affect your daily life. It will take approximately 15 minutes to complete. This is for research.

- **Review of health status** – this will include a review of your medical and hospitalization history, a list of the medications you are taking, past culture results, and demographic information (birthdate, gender). A CF physician will perform a physical exam as part of your care while hospitalized. Your vital signs, like height, weight, temperature, and blood pressure will also be measured. This is part of your clinical care. We would like to look at the results for research.

- **Results from your spirometry** (lung function testing) – this is a breathing test that measures the amount of air in your lungs and how forcefully you can blow the air into a machine. This is part of your clinical care. We would like to look at the results for research.

- **Results from laboratory tests** – this will include blood and urine tests. Serum chemistry, a measurement of several substances in your blood, and serum creatinine, a measure of how well your kidneys are working, will be measured from your blood. Your urine will be tested for protein to measure how well your kidneys are working. If you are female, a pregnancy test will also be done. This is part of your clinical care. We would like to look at the results for research.

- **Results from your sputum (mucus) sample** – this will allow us to see what bacteria and how much bacteria are growing in your airways. This is part of your clinical care. We would like to look at the results for research.

The table below shows you the schedule of events. Depending on the treatment you are randomized to, you will have blood or blood and sputum collected on visits 2 and 3. T refers to IV Tobramycin treatment; C refers to IV Colistin treatment; X refers to all study subjects, regardless of treatment. The → means that we will collect the results from your clinical care lab tests throughout your participation in the study, not just on the study visits.

	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**
Informed Consent and Eligibility Review	X			
Demographics	X			
Medical History and Concomitant Medications	X			X
Physical Exam and Vital signs	X	X	X	X
Questionnaires	X			X
Spirometry	X			X
Blood labs	→	→	→	→
Urine labs	→	→	→	→
Sputum microbiology	X			X
Blood collection for pharmacokinetic analysis (PK)		T, C	T, C	
Sputum collection for pharmacokinetic analysis (PK)		C	C	
Urine collection for pharmacokinetic analysis (PK)		C	C	
Urine collection for Nephrocheck	X	X	X	X

How will my samples be used?

Blood samples – your blood will be processed in the laboratory and the amount of antibiotic in the sample will be measured on a machine called a mass spectrometer.

Sputum samples – your sputum will be processed in the laboratory and the amount of antibiotic in the sample will be measured on a machine called a mass spectrometer.

Urine samples – one-half of your urine will be processed in the laboratory and the amount of antibiotic in the sample will be measured on a machine called a mass spectrometer. The other half will be frozen and stored in a laboratory freezer. If you have an abnormal blood test (high serum creatinine), your urine will be thawed and tested for kidney damage using a FDA approved assay kit called Nephrocheck®.

We will not put your name on any research specimen or data. Instead, we will label your samples and personal information with a study number. The list that links your name to study number is stored separately from the research specimens. Your samples will be used only for this study and will be kept until the study is over.

What are the possible risks and side effects of the study?

Medications: No new or experimental drugs are being used in this study, and no medications are being withheld. However, you may be randomized into a modified IV colistin dosing schedule where the dosing is changed based on how your body is absorbing the drug. This is experimental.

Side effects that rarely occur with the use of IV tobramycin include ototoxicity and vestibular toxicity (hearing damage) and nephrotoxicity (kidney damage). You may feel dizzy or have a ringing in your ears. You should report any symptoms you may feel to your doctor immediately. Daily blood tests will measure for any possible kidney damage. Though rare, these side effects can occur in 1 out of 5 patients. Side effects that rarely occur with the use of IV colistin include nephrotoxicity and neurotoxicity (kidney damage and nerve damage). You may feel dizzy or weak. You should report any symptoms you may feel to your doctor. Daily blood tests will measure for any possible kidney damage. Though rare, these side effects can occur in 3 out of 10 patients.

Toxicities from tobramycin and colistin are usually, though not always, reversible when the agent is stopped.

Blood draw: Whenever possible, the research blood specimens will be obtained when blood is drawn for clinical laboratory tests ordered for care by your CF doctor. In that case, this will not involve any extra needle pokes for you. If this is not possible, blood will be removed by putting a needle into your vein. This is the standard method used to obtain blood for tests. There is a risk you will feel pain when the needle goes into the vein. A bruise may form at the site. The use of numbing cream is optional and may decrease discomfort. Blood may also be drawn through your PICC line or a Medi-port, if you have one. Discuss all side effects with your study doctor and your regular doctor.

Pulmonary function tests: The lung function tests may be associated with coughing or you may feel lightheaded.

Expectorated sputum: There is a risk of chest tightness or wheezing.

Questionnaire: There is a risk of feelings of anxiety. You make skip any questions that make you feel uncomfortable.

There is the risk of loss of privacy and confidentiality from participating in the study. All data will be coded; your name will not be given to any other researcher. Only the Principal Investigator (Dr. Saavedra) and Research Coordinator will have access to the code which links patient identification to specimens.

It is not expected that study participants will have all of these side effects. The study may include risks that are unknown at this time.

What happens if I am hurt or become ill during the study?

In the event of an injury or illness resulting from your participation in this research study, your study doctor will assist you in receiving appropriate health care, including first aid, emergency treatment and follow-up care either at National Jewish Health, National Jewish Health │ Saint Joseph Hospital, or another appropriate health care facility. If medical costs are incurred, your insurance company may be billed. In accordance with general policy, National Jewish Health and National Jewish Health │ Saint Joseph Hospital make no commitment to provide free medical care or other compensation for injury or illness resulting from your participation in this study. By signing this form, you have not given up your legal rights. For further information, please contact Dr. Milene Saavedra, the Principal Investigator of this study.

If you believe you have experienced any study related illness, adverse event, or injury, you must notify the study doctor as soon as possible.

This has been explained to me and all my questions have been answered.

_____
Subject's Initials

Are there any possible benefits to being in the study?

If you agree to take part in this study, there may or may not be direct medical benefits to you. Your condition may or may not improve by participating in this study. By reducing the number of doses of IV colistin, there will be less accumulation of the drug, which may lead to reduced risk of kidney damage.
Knowledge gained from the study may benefit future patients with CF. This study may alter the recommendations of IV antibiotic treatment for pulmonary exacerbations, reducing hospital stays and improving quality of life.

What other choices do I have?

You can choose not to participate in this study. Your participation is voluntary and will not affect the care provided to you at National Jewish Health or National Jewish Health │ Saint Joseph Hospital. If you have any questions about the research or your participation, you should contact one of the researchers on the study. You are not obligated for any reason to participate in this study and can choose to not participate at any time.

Other IV antibiotic treatments for an APE exist. You should talk about these treatments with your doctor before you decide to take part in the study. You may choose to not take part in the study.
The treating clinician may be both your health care provider and the investigator for this study. This clinician is interested both in your clinical welfare and in the conduct of this study. Before entering this study, or at any time during the study, you may ask for a second opinion about your care from another clinician who is not associated in any way with this study.

Who is paying for this study?

The CF research team at National Jewish Health is receiving funding from The Cystic Fibrosis Foundation for this study.

Will I have to pay for anything?

Since you are admitted to the hospital as an in-patient while taking part in this study, you or your insurance company may incur costs for expenses NOT directly related to the study. You will not have to pay for any research procedures.

Will I be paid for being in the study?

You will be paid $20 for each visit in this study. This will add up to a total of $80 if you complete all of the visits. If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed.

Patient confidentiality will be protected in accordance with the requirements of the Health Insurance Portability and Accountability Act (HIPAA). However, because CF is a rare disease, please note that if you are currently receiving SSI, Medicaid or Medicare low-income subsidies, you are currently able to receive up to $2000 in a calendar year as payment for study participation without it affecting your continued eligibility for these benefits. If you have any questions, please feel free to ask.

Is taking part in the study voluntary?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to stop later, you will not lose any benefits or rights to which you are entitled.

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm. If your CF physician or other clinical providers believe that it is appropriate to have you continue in the study, this will be allowed. If study drug is stopped, the data collected up to this point will be used in the analysis. You may be taken out of the study even if you do not want to leave the study.

The sponsor, the Cystic Fibrosis Foundation, may stop the study at any time.

Who do I call if I have questions or problems?

You may ask any questions you have at this time. If you have questions, concerns, or complaints later, you may call the research coordinator at 303-398-1255 or Dr. Saavedra at 303-270-2333

If you have questions or concerns about your rights as someone in this study, please call the National Jewish Health Institutional Review Board (IRB) at 303-398-1477.

Who will see my research information?

National Jewish Health has rules to protect information about you. Federal and state laws, including the Health Insurance Portability and Accountability Act (HIPAA), also protect your privacy. This part of the informed consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- *National Jewish Health*
- *National Jewish Health | Saint Joseph Hospital*

We cannot do this study without your permission to see, use and give out your information. You do not have to give us permission. If you do not, then you may not join the study.

We will see, use and share your information only as described in this form and in our Notice of Privacy Practices; however, people outside National Jewish Health may not be covered by this promise.

We will do everything we can to keep your records private. It cannot be guaranteed. At minimum, we will your research records will be stored in a locked office with limited access and secure computer files. We will not put your name on any research specimen or data. Instead, we will label your samples and personal information with a study number. The list that links your name to study number is stored separately in a securely locked research office and on a secure computer file.

The use and sharing of your information has no time limit. You can withdraw your permission to use and share your information at any time by writing to the Corporate Compliance Officer at the address listed below. If you do withdraw your permission, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected for the study.

Corporate Compliance Officer
National Jewish Health
1400 Jackson Street M113a
Denver, CO 80206

The records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information. Your information may be shared with:

- The study doctor and his/her team of researchers
- The Cystic Fibrosis Foundation, the company paying for this research study

- Officials at National Jewish Health who are in charge of making sure that we follow all of the rules for research
- National Jewish Health Institutional Review Board (IRB), the ethics board responsible for overseeing this research
- Department of Health and Human Services

We might talk about this research study at meetings. We might also print the results of this research study in medical journals or medical magazines. But we will always keep the names or other information that could identify you private.

You have the right to request access to your personal health information from the Investigator, National Jewish Health, or National Jewish Health | Saint Joseph Hospital. Test results and other medical information gathered in this study will be stored in your research study file and will be treated with the same confidentiality as other medical records here at National Jewish Health as required by state and federal regulations.

Information about you that will be seen, collected, used, and shared in this study:

- Name and demographic information (age, sex, ethnicity, etc.)
- Portions of your previous and current medical records that are relevant to this study, including but not limited to diagnosis(es), history and physical, laboratory or tissue studies, radiology studies, procedure results
- Research visit and research test records
- Blood/tissue samples and the data with the samples

What happens to Data, Tissue, Blood and Specimens that are collected in this study?

Scientists at National Jewish Health work to find the causes of and cures for disease. The data, tissue, and blood specimens collected from you during this study are important. If you join this study:

- The data, tissue, blood, or other specimens given by you to the investigators for this research no longer belong to you.
- The investigators and any sponsor of this research may study your data, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, National Jewish Health or other organizations involved in this study may use them only in a manner consistent with this form and with Institutional Review Board approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

Agreement to be in this study and use my data

I have read and initialed each page of this informed consent and HIPAA authorization form (or it was read to me). I was informed about the possible risks and benefits of being in this study. I know that being in this study is voluntary. I choose to be in this study. I know I can stop being in this study at any time. I will get a copy of this form after it is signed.

Signature of Participant	Date	Printed Name of Participant
Signature of Person Obtaining Consent	Date	Printed Name of Person Obtaining Consent