

## **Immune Enhancement for Immunological Non-responders to ART**

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**NCT01806870**

**Emory University**  
**Consent to be a Research Subject**

**Title:** Immune Enhancement for Immunological Non-responders to ART

**Principal Investigator:** David Guidot, MD

**Sponsor:** National Institutes of Health

**Introduction**

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. law. This Web site will not include information that can identify you. At most the Web site will include a summary of the results. You may search this Web site at any time.

**Study Overview**

The purpose of this study is to see if taking two nutritional supplements, zinc and SAME (S-adenosylmethionine), can improve lung health and immune function in persons with HIV. You are being asked to volunteer because you have HIV (Human Immunodeficiency Virus) and you take anti-retroviral therapy (ART) medications.

We plan to enroll about 20 volunteers from the Grady Health System and about 60 nationwide. Your time in the study will last about 15 months.

Both zinc and SAME supplements are commercially available over-the-counter. However, they are not currently regulated by the US Food and Drug Administration (FDA). The use of these supplements for this research study is considered experimental.

**Procedures**

There will be up to eleven study visits and three telephone visits. Study visits will be done at the Grady Ponce De Leon Center, Grady Medicine Clinic, and at Grady Hospital. All study procedures are for research purposes. All study subjects will receive the nutritional supplements zinc and SAME.

During the study you will be asked to answer questions about your alcohol use and smoking history. You will have exhaled breath tests, blood draws, physical exams, and bronchoscopies. Your medical records will be reviewed during the study. If you are a woman of childbearing age, a urine pregnancy test will be done at each study visit.

**Visit 1 (screening visit):** This visit will last about 2 hours and will take place at either Grady Ponce De Leon Center or Grady Medicine Clinic. At this visit you will:

- Have a physical exam
- Review your medical history
- Review your medications
- Have blood drawn
- Have a urine pregnancy test for women of child-bearing age
- Complete a survey about your alcohol use and smoking history.
- Discuss and schedule a bronchoscopy for the next visit

You may not be eligible to continue in the study if the blood work done at visit one is not within normal limits or if you are pregnant. A study team member will contact you to let you know if you do or do not qualify to participate in the remainder of the study.

**Visit 2:** This visit will last about 6 hours and will take place at Grady Hospital. At this visit you will:

- Have a physical exam
- Have blood drawn
- Have a urine pregnancy test for women of child-bearing age
- Do an exhaled breath test
- Have a bronchoscopy
- Receive nutritional supplements and education

**Treatment:** The nutritional supplements zinc and SAME will be given to you by the study team at visit 2. You will be asked to take one tablet once a day.

If you experience upset stomach, abdominal cramps, diarrhea, or other uncomfortable side effects, we will reduce the amount of the nutritional supplements. If your symptoms do not improve, we will continue to decrease the amount of nutritional supplements taken by you. If you are unable to tolerate the nutritional supplements, you will be withdrawn from the research study.

**Visits 3, 4, and 5 -Telephone Contact:** You will receive a telephone call at one, two, and three weeks after visit 2 to ask you how you are tolerating the study supplements. If you are experiencing side effects such as upset stomach, abdominal cramps, or diarrhea, we will instruct you to decrease the dose of the supplements.

**Visits 6, 7, and 8 (months one, two, and three):** These visits will last about 30 minutes and will be scheduled two months apart. They will take place at either Grady Ponce De Leon Center or Grady Medicine Clinic. At this visit you will:

- Have blood drawn
- Have a urine pregnancy test for women of child-bearing age
- Do an exhaled breath test
- Answer questions about how you are tolerating the nutritional supplements
- Receive nutritional supplements and education

If your exhaled breath test is at goal at visit 6, you will continue to take the dietary supplements for one year from this point forward. If your exhaled breath test is not at goal at visit 6, you will be asked to return for visit 7. If your exhaled breath test is at goal at visit 7, you will continue to take the dietary supplements for one year from this point

forward. If your exhaled breath test is not at goal at visit 7, you will be asked to return for visit 8. You will be asked to take the nutritional supplements for one year from this point forward.

**Visits 9 through 13:** These visits will last about 30 minutes and will be scheduled two months apart. They will take place at either Grady Ponce De Leon Center or Grady Medicine Clinic. At this visit you will:

- Have blood drawn
- Have a urine pregnancy test for women of child-bearing age
- Answer questions about how you are tolerating the nutritional supplements
- Receive nutritional supplements and education
- You will receive an exhaled breath test at visit 9 and visit 11

**Visit 14:** This is the final study visit. It will last about 6 hours and will take place at Grady Hospital. At this visit you will:

- Have a physical exam
- Have blood drawn
- Have a urine pregnancy test for women of child-bearing age
- Do an exhaled breath test
- Have a bronchoscopy procedure
- Return unused nutritional supplements

The following describes the tests and procedures that will be done in this study:

1. **Physical exam:** A medical doctor will perform a brief physical exam that will include evaluating your nose and throat and listening to your lungs and heart. You will also be asked about any problems you may have had with previous medical procedures. You will be asked what medications you are currently taking.
2. **Blood collection:** Your blood will be drawn (about 3 tablespoons) between nine and eleven times. These samples will be used for different types of testing that will help us better understand your immune function. In addition, your blood may be used for DNA testing and stored for future use at Emory University, Atlanta, Georgia. A separate consent form will be presented to you for this optional sub-study.
3. **Exhaled breath collection:** This test involves breathing normally into a chilled tube for 10 minutes to collect your breath. This will be done between 3 and 5 times. You will be asked not to eat or smoke for 3 hours before this test.
4. **Survey:** You will be asked questions about your alcohol use and your smoking history. This will be done once. It will take about 20 minutes to complete.
5. **Bronchoscopy:** This procedure will be done two times, before starting the supplements and then again about 1 year later. Your bronchoscopy will be done by a highly trained pulmonary (lung) doctor, who may or may not be a member of this study. The bronchoscopy only takes about 20 minutes, but the entire procedure will take around 5 hours. This includes time to prepare and recover. The following will occur during the procedure:
  - The procedure:
    - You will be asked not to eat or drink anything for at least six hours before the bronchoscopy.
    - Your nose and throat will be coated with a numbing medicine.
    - You will have an IV inserted into your arm or hand.
    - You will get a sedative through a needle in the IV so you are relaxed and comfortable.
    - You will have a flexible tube called a bronchoscope passed through your nose or mouth into the throat and into your lungs.
    - After the tube is in your lungs, up to two areas of your lung will be rinsed with salt water and fluid will be collected (about 9 teaspoons).
  - The recovery:
    - You will rest for about 2 or 3 hours until you are alert and no longer sleepy
    - You will be given something to drink to make sure you are able to swallow liquids

- You will not be allowed to drive home. You must have someone available to drive you home.
- You will be instructed to rest at home for the rest of the day.
- You should be able to return to your normal activities the next day.

Summary of your visits and the procedures you will have at each visit:

Procedures	V1	V2	V3	V4	V5	V6 (1 month)	V7 (at 2 months if needed)	V8 (at 3 months if needed)	V9	V10	V11	V12	V13	Visit 14 Final visit
Informed Consent	X													
Physical Exam	X	X												X
EBC		X				X	X	X	X	X	X			X
Blood work	X	X				X	X	X	X	X	X	X	X	X
Alcohol use and Smoking Survey	X													
Bronchoscopy		X												X
Urine pregnancy test (for women)	X	X				X	X	X	X	X	X	X	X	X
Dispense and/or adjust supplements		X	X	X	X	X	X	X	X	X	X	X	X	
Adverse Events		X	X	X	X	X	X	X	X	X	X	X	X	X
Telephone contact			X	X	X									

**Risks and Discomforts**

**If you are a woman:** to protect against possible side effects of the nutritional supplements, women who are pregnant or nursing a child may not take part in this study. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

If you will be taking the study drug home, keep it out of the reach of children or anyone else who may not be able to read or understand the label. Do not let anyone else take the study drug besides you.

**Risks of Blood Drawing-** May cause faintness, swelling of the vein, pain, bruising, or bleeding at the site of puncture, and a slight chance of infection.

**Risks of Exhaled Breath Collection** - There are no known risks for this procedure.

**Risks of Bronchoscopy with Bronchoalveolar Lavage (BAL)** - You will undergo bronchoscopy with BAL two times during this study. This procedure can be uncomfortable. It may make you feel like you have to cough. It may cause minor irritation in your lungs. This does not usually hurt your lungs. Bronchoscopy with BAL can also cause the level of oxygen in your blood to drop. To reduce the chance of this happening, we will give you oxygen and check your oxygen level continuously during the procedure. We will also stop the procedure or give you immediate treatment if your oxygen

level drops too low. Another possible side-effect is fever in the 24 hours after the test (8%). There is a very small chance - less than 1% - that you could experience bleeding in the lungs (0.7%), wheezing (0.7%), or that your lung could be seriously injured or collapsed during BAL. There is a risk of respiratory failure and even death from bronchoscopy or from sedation and local anesthetics used during bronchoscopy (1 to 2 in 10,000).

**Risks of Conscious Sedation** - You will be given medications through your IV to relax you during the bronchoscopy. This will allow you to better tolerate the procedure. The medications that will be given are a benzodiazepine (sedative) and an opiate (suppresses cough and relieves discomfort). No long lasting effects on memory have been reported from these types of medicines, but harmful side effects that could happen include: hiccups (3.9%), nausea (2.8%), vomiting (2.6%), coughing (1.3%), headache (1.5%), drowsiness (1.2%), acute shortness of breath (<1%), heart problems (e.g. low blood pressure)(<1%), and anaphylactoid or allergic reactions (<1%). You will be closely monitored while receiving these medications. If any of these risks should occur, you will be treated immediately.

**Risks of Lidocaine** - Lidocaine is the medication used to numb your mouth and airway. It is often bitter and may cause a stinging sensation before the skin becomes numb. Very rarely, it may be associated with confusion (<0.01%), local allergic skin reactions (<0.1%), heart rhythm changes (<0.001%), or seizures (<0.01%).

**Risks from taking zinc supplements** - Zinc is a naturally occurring mineral that is important for growth and development of body tissues. Zinc supplements are readily available over-the-counter and are relatively safe, but as with any other supplement, you may experience some side effects. Common side effects (<10%) are: dizziness, headache, abdominal cramps, diarrhea, nausea, and vomiting. In a recent study, zinc supplements did not cause any significant side effects in people living with HIV even over an 18 month period. However, the doses used in that study were about half of the starting dose that you will take in this study. We estimate that the risk of significant side effects is less than 10% with this higher dose, but we will watch closely for side-effects and can reduce the dose in half if necessary. If you cannot tolerate half of the planned starting dose, then you will be excused from the study. Even though allergic reactions to zinc are very rare, you should be aware of the symptoms in case you experience them. These symptoms include hives, difficulty breathing, and swelling of your face, lips, tongue, or throat. You will need emergency treatment if any of these symptoms occur. There is a chance that zinc will interact with other medications, so it is important that the study physicians are aware of all medications that you are currently taking.

**Risks from taking S-adenosylmethionine (SAME)** - SAME is the synthetic form of a compound that is formed naturally in the body. It is available as a nutritional supplement and is relatively safe for most people. The most common side effects are digestive complaints such as nausea, gas, and upset stomach. Other side effects are less common and include skin rash, dry mouth, headache, mild insomnia, anorexia, sweating, dizziness, and nervousness. The side effects are more common at higher doses, so it is important that you take the supplement only as prescribed by the study doctor. SAME can cause mania in people with bipolar disorder and worsen the symptoms of Parkinson's disease. You are disqualified from participating in the study if you have either of these conditions. SAME may also increase bleeding risk. Therefore, you should not have any scheduled surgery until at least two weeks after stopping the supplement. You would also not be able to participate in this study if you have a bleeding disorder.

**Unknown risks in taking dietary supplements:** This study involves taking supplements, and you may experience side effects that have not been previously reported, so it is important that you report any new symptoms that you experience after starting the study supplements.

**Unknown Risks:** There may be risks, discomforts or side effects that are not yet known. Tell the doctor or study staff if you are experiencing any problems.

**New Information**

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

**Benefits**

This study is not designed to benefit you directly. Your HIV may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about zinc and SAME (S-adenosylmethionine), and if taking them can improve lung health and immune function in persons with HIV. The study results may be used to help others in the future.

**Compensation**

You will be compensated for each completed study visit. If you do not finish the study, you will be paid for the visits you have completed. You will receive \$525 total, if you complete all study visits.

You will be compensated for your time and inconvenience. At visits 2 and visit 14 you will receive cash and a gift card will be given for the other visits.

Visits 1:	\$ 25
Visits 2:	\$ 150
Visits 6 through 13:	\$ 25
Visit 14:	\$ 150

Please note: You will not be compensated for visits 7 and/or 8 if you are told you do not need to report for those visits. You will also not be compensated for missed visits.

Please note that Emory University is required to complete form 1099 for any participant payments over \$600. To comply with this federal mandate the researchers are required to obtain your social security number to complete the form.

**Confidentiality**

Certain offices and people other than the researchers may look at your medical charts and study records. Government agencies and Emory or Grady Health System employees overseeing proper study conduct may look at your study records. These offices include the Office for Human Research Protections, the Emory or Grady Health System Institutional Review Board, the Emory or Grady Health System Office of Research Compliance, the Office for Clinical Research, the Clinical Trials Audit & Compliance Office. The National Institute of Health, the study sponsor, may also look at your study records. The Data Safety and Monitoring Board may look at your records. This board is comprised of faculty from Emory University and University of Washington. Emory or Grady Health System will keep any research records we create private to the extent we are required to do so by law. A study number rather than your name will be used on study records wherever possible. Your name and other facts that might point to you will not appear when we present this study or publish its results.

Study records can be opened by court order. They may also be produced in response to a subpoena or a request for production of documents.

Research Information Will Go Into the Medical Record:

If you are or have been an Emory or Grady Health System patient, you have an Emory or Grady Health System medical record. If you are not and have never been an Emory or Grady Health System patient, you do not have one. Please note that an Emory or Grady Health System medical record will be created if you have any services or procedures done by an Emory or Grady Health System provider or facility for this study.

If you agree to be in this study, a copy of the consent form and HIPAA patient form that you sign will be placed in your Emory or Grady Health System medical record. Emory or Grady Health System may create study information about you that can help Emory or Grady Health System take care of you. For example, the results from some of the blood tests may be placed in your medical record. These useful study results will be placed in your Emory or Grady Health System medical record. Anyone who has access to your medical record will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA Privacy Rule. On the other hand, some state and federal laws and rules may not protect the research information from disclosure.

Emory or Grady Health System does not control results from tests and procedures done at other places, so these results would not be placed in your Emory or Grady Health System medical record. They will not likely be available to Emory or Grady Health System to help take care of you. Emory or Grady Health System also does not have control over any other medical records that you may have with other healthcare providers. Emory or Grady Health System will not send any test or procedure results from the study to these providers. If you decide to be in this study, it is up to you to let them know.

The researchers will review the results of certain study tests and procedures only for the research. The researchers will not be looking at the results of these tests and procedures to make decisions about your personal health or treatment. For this study, those things include: the exhaled breath test, bronchoalveolar lavage and some of the blood tests.

***There is a Certificate of Confidentiality for this Study:***

We will do everything we can to keep others from learning about your participation in the research. To further help protect your privacy, the investigator has applied for a Certificate of Confidentiality.

***What the Certificate of Confidentiality protects:***

The National Institutes of Health has given this study a Certificate of Confidentiality. Emory or Grady Health System would rely on it to not give out study information that identifies you. For example, if Emory or Grady received a subpoena for study records that identify you, we would say no. The Certificate gives Emory or Grady Health System legal backup to say no. It covers information about you that could harm your image or finances. It also covers information about you that could harm your chances at a job or getting insurance.

***What the Certificate of Confidentiality does not protect:***

The Certificate does not prevent you or someone other than you from making disclosing your information. The Certificate also does not prevent Emory or Grady from releasing information about you:

- Information to state public health offices about certain infectious diseases
- Information to law officials if child abuse has taken place
- Information Emory or Grady gives to prevent immediate harm to you or others
- Information Emory or Grady gives to the study sponsor as part of the research

**In Case of Injury**



*If you get ill or injured from being in the study, Emory or Grady Health System would help you to get medical treatment. Emory or Grady Health System have not; however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proved that your injury or illness is directly caused by the negligence of an Emory or Grady Health System employee. "Negligence" is the failure to follow a standard duty of care.*

*If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.*

*If you believe you have become ill or injured from this research, you should contact Dr. David Guidot at telephone number (404) 712-2970. You should also let any health care provider who treats you know that you are in a research study.*

### **Costs**

There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities.

### **Withdrawal from the Study**

You have the right to leave a study at any time without penalty. For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interest;
- You were to object to any future changes that may be made in the study plan;
- You are unable to tolerate the nutritional supplements
- or for any other reason.

### **Contact Information**

Contact David Guidot,, MD at (404) 712-2970

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or [irb@emory.edu](mailto:irb@emory.edu):

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at <http://www.surveymonkey.com/s/6ZDMW75>.

You may also contact Dr. Curtis Lewis, Senior Vice President for Grady Health System Medical Affairs at (404) 616-4261.

### **Consent**

Please, print your name and sign below if you agree to be in this study. By signing this consent form, you will not give up any of your legal rights. We will give you a copy of the signed consent, to keep.

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Name of Subject

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Signature of Subject

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Date          Time

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Signature of Person Conducting Informed Consent Discussion

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Date          Time

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Name of Person Conducting Informed Consent Discussion

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Date          Time