

SOASUMMARY OF CHANGES
A Phase II Study of sEphB4-HSA in Kaposi Sarcoma
Version 6.0

NCI Protocol #: AMC-096
Local Protocol #: AMC-096

NCI Version Date: 31AUG2023
Protocol Date: 31AUG2023

I. Administrative and Editorial Changes

#	Section	Comments
1.	Global	The informed consent form was updated from version 5.0 to version 6.0 and the date was updated from 20JUL2023 to 31AUG2023.
2.	What extra tests and procedures will I have if I take part in this study	The study calendar was updated to align with the schedule of events specified in the protocol document.
3.	What are the costs of taking part in this study?	The visit titles were updated to align with the protocol; additionally, the number of post treatment evaluation visits was updated from 5 to 4, in order to be consistent with the protocol.

AMC-096 MODEL INFORMED CONSENT FORM

Study Title for Study Participants: **A Study of sEphB4-HSA in Kaposi Sarcoma**

Official Study Title for Internet Search on <http://www.ClinicalTrials.gov>: **A Phase II Study of sEphB4-HSA in Kaposi Sarcoma**

A Clinical Trial of the AIDS Malignancy Consortium (AMC)

WHAT IS THE USUAL APPROACH TO KAPOSI SARCOMA?

You are being asked to take part in this study because you have Kaposi sarcoma which has grown or has recurred. People who are not in a study are usually treated with either topical medication, radiation, or with systemic chemotherapy drugs. Sometimes, combinations of these are used and your doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or more.

WHAT ARE MY OTHER CHOICES IF I DO NOT TAKE PART IN THIS STUDY?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for Kaposi sarcoma

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to test any good and bad effects of the study drug called sEphB4-HSA. Researchers hope to learn if the study drug will decrease the number or size of Kaposi sarcoma lesions in people. This drug is considered an experimental drug because it has not been used in people with Kaposi sarcoma. This drug has not been approved by the Food and Drug Administration (FDA) for treatment of cancer. It has shrunk several types of cancer in animals. It has been used in human clinical trials for other types of cancer. There will be about 20 people with Kaposi sarcoma taking part in this study.

WHAT ARE THE STUDY GROUPS?

All study participants will be in the same study group and get the same study medication. All study participants will receive an intravenous infusion (medicine through a needle in a vein in your arm) of sEphB4-HSA. All treatment will be performed in the outpatient setting. Each cycle of the study drug sEphB4-HSA will be 4 weeks. All participants will begin the study at the same dose level. You will receive two 10 mg/kg doses of study drug on Days 1 and 15.

HOW LONG WILL I BE IN THIS STUDY?

Up to 2 years. You will receive sEphB4-HSA for a maximum of 12 four-week cycles, or 48 weeks. The length of time you will be on the drug depends on how well you tolerate the study drug (i.e., if you have any significant side effects that require us to stop treatment), and how well the drug is working against the Kaposi sarcoma. You will receive one extra cycle of treatment if all signs of KS disappear. Your doctor will continue to watch you for side effects and follow your condition for at least 4 weeks and up to one year after your last dose, depending on whether your KS responded to the study drug. If your KS lesions completely disappeared during treatment and then get worse after stopping treatment, the study doctor may start study treatment again. If your KS is

stable or better, you will be followed every three months for up to one year, or until you go on another treatment for KS.

WHAT EXTRA TESTS AND PROCEDURES WILL I HAVE IF I TAKE PART IN THIS STUDY?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra procedures including imaging, blood tests, exams, and biopsies that you will need to have if you take part in this study.

Before you begin the study you will have the following:

You will need to have the following extra imaging, blood tests, exams, and biopsies to find out if you can be in the study:

- Photographs of your Kaposi sarcoma lesions
- Documentation of HIV status
- We will ask questions related to the risk of getting HIV, including drug use and sexual behavior.
- If HIV positive, CD4 counts
- Blood tests to evaluate baseline blood counts, electrolytes, and liver function tests
- Blood samples for research
- Urine samples
- Pregnancy test for females of childbearing potential
- Chest X-ray (CXR)
- Computerized tomography (CT) scan. This would only be needed if you have any respiratory symptoms or a specific finding on your CXR. A CT scan uses computerized X-rays to make virtual slices of specific parts of the body.
- Biopsies of your Kaposi sarcoma lesions
- A survey about your quality of life in regards to Kaposi sarcoma
- An electrocardiogram (EKG), a test to measure the electrical activity of the heart

Biopsies of your Kaposi sarcoma lesions will be taken for the study. The biopsies will be taken before you begin the study drug, and after two doses of the study drug. This sample is required in order for you to take part in this study because the research on the sample is an important part of the study. The research biopsy is done in a similar way to biopsies done for diagnosis. The biopsies will be used for study purposes. We hope to look at changes to different proteins important to the development and activity of Kaposi sarcoma.

Part of the specimen will be stored for biobanking. This will allow us to do further studies on the tumor after the study is complete. A biobank is a facility that stores human biological samples for use in research.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. The study results may be available to your study doctor at a later point in time.

Neither you nor your health care plan/insurance carrier will be billed for the collection of the extra imaging, blood tests, exams, and biopsies that will be used for this study.

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra imaging, blood tests, exams, and biopsies. They are not part of the usual approach for your type of cancer.

During the study, you will receive:

- Physical exams and questions regarding your medications and symptoms before the first two doses of study drug, and then before every cycle of study drug
- Photographs of your Kaposi sarcoma lesions before every cycle
- If HIV positive, peripheral blood tests to measure HIV viral loads and CD4/CD8 counts every three months
- Blood tests to evaluate baseline blood counts, electrolytes, liver function tests before each dose of study drug
- Urine samples to check for the amount of protein in your urine
- Pregnancy test for females of childbearing potential
- Blood samples for research. This will include blood samples to check the level of the drug every week during the first and second cycle, as well as blood samples for research before each dose of study drug during the first cycle, and before each cycle of study drug thereafter
- Biopsies of your Kaposi sarcoma lesions after two doses of the drug
- A survey about your quality of life in regards to Kaposi sarcoma while on the study drug
- If you have Kaposi sarcoma lesions inside your body, you may have extra scans to evaluate any changes in those lesions

A study calendar that shows how often these exams, tests, and procedures will be done is below.

You will receive sEphB4-HSA every 2 weeks in this study. Four weeks of time is called a cycle. The cycle will be repeated for a maximum of 12 times. Each cycle is numbered in order. The chart below shows what will happen to you during Cycle 1 and future treatment cycles as explained previously.

The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

Cycle 1

For all Study Participants

Day	What you do
Before starting the study	<ul style="list-style-type: none"> • Review and sign informed consent form • Medical history and physical exam • Kaposi sarcoma tumor assessment, including KS tissue biopsy and photographs of KS lesions • Chest X-ray • If HIV positive, CD4 and CD8 counts, and HIV-1 plasma RNA • Get blood tests • Urine samples • Pregnancy test for females of child-bearing age • Quality of life survey

Day	What you do
	<ul style="list-style-type: none"> • If required, a Computerized Tomography (CT) scan
Day 1	<ul style="list-style-type: none"> • Physical exam and medical review • Kaposi sarcoma tumor assessment, including KS tissue biopsy and photographs of KS lesions • If HIV positive, CD4 and CD8 counts, and HIV-1 plasma RNA • Get blood and urine tests • Pregnancy test for females of child-bearing age • Quality of life survey • Receive sEphB4-HSA dose
Day 15	<ul style="list-style-type: none"> • Physical exam and medical review • • Get blood tests • Pregnancy test for females of child-bearing age • Quality of life survey • Receive sEphB4-HSA dose • KS tissue biopsy after dose of sEphB4-HSA

Future Cycles 2-12

For Doses Administered on Days 1 and 15

Day	What you do
Day 1	<ul style="list-style-type: none"> • Physical Exam and medical review • Kaposi sarcoma tumor assessment and photographs of KS lesions • Get blood and urine tests • If HIV positive, CD4 and CD8 counts, and HIV-1 plasma RNA (cycles 4, 7, and 10 only) • Receive sEphB4-HSA dose
Day 15	<ul style="list-style-type: none"> • Physical Exam and medical review • Get blood tests • Quality of life survey (cycle 4 only) • Receive sEphB4-HSA dose

After Completing All Treatment or Ending Treatment on this Study

Day	What you do
Approximately 1 month after treatment	<ul style="list-style-type: none"> • Physical exam and medical review • Kaposi sarcoma tumor assessment and photographs of KS lesions • Get blood and urine tests • If HIV positive, CD4 and CD8 counts, and HIV-1 plasma RNA • Quality of life survey

If you are responding to treatment, you will have additional physical exams, medical reviews and evaluations of your lesions repeated every 3 months for up to 1 year.

WHAT POSSIBLE RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

If you choose to take part in this study, there is a risk that:

- You may have side effects from the drug
- You may be asked to start medications if you have higher than normal blood pressure and risk factors for higher blood pressure prior to and while on the study drug, as high blood pressure can be a side effect of this study drug
- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

The study drug sEphB4-HSA used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor and/or the research team about additional medicines that you are taking such as prescribed/herbal drugs, over-the-counter medicines, or alternative medicines.
- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The table below shows the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about given there have been relatively few trials using this particular drug. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects Of sEphB4-HSA

POSSIBLE, SOME MAY BE SERIOUS
<ul style="list-style-type: none">• Bleeding• Nausea• Vomiting• Coughing up blood• Fever

POSSIBLE, SOME MAY BE SERIOUS
<ul style="list-style-type: none"> • Syncope (or fainting) • Chills • Rigors (or shakes) • Itching or rash at the site of the infusion • Allergic reactions that may include skin swelling and/or swelling of the face or throat and could be severe or life threatening • Difficulty breathing • Increased levels of blood potassium • Increased levels of uric acid (a waste material from food digestion) • Increased levels of phosphate • Decreased levels of blood calcium • Kidney damage and kidney failure • Decreased platelet count • Lack of enough red blood cells • Decrease in the total number of white blood cells • Increased number of white blood cells • Muscle pain, inflammation and weakness • Joint pain, and inflammation • Stoppage of blood flow to your brain • Changes in the brain that may cause convulsions and confusion • High blood pressure (new or worsened, if pre-existing) • Low blood pressure • Irregular heartbeat • Heart attack • Tiredness • Headaches • New or worsening heart failure that can show up as feeling short of breath, swelling in the legs, and/or chest pain or decreased heart function (including cardiac arrest), and can uncommonly be severe or fatal. If you have heart failure, you should tell your doctor.

Additional Study Risks

Biopsies: Common side effects of a biopsy are a small amount of bleeding at the time of the procedure, pain at the biopsy site, which can be treated with regular pain medications, and bruising. Rarely, an infection can occur. You will sign a separate consent form before the biopsy is taken. This will be a standard surgical consent form from the institution where the biopsy procedure takes place.

Pregnancy and Breastfeeding: sEphB4-HSA could potentially harm a fetus or a nursing baby. Women who are pregnant or breastfeeding cannot take part in this study. Women must agree to not breastfeed during the study or for at least 28 days after stopping sEphB4-HSA. Women should not take sEphB4-HSA if they are pregnant or planning to become pregnant. Men should not father a baby while taking study treatment. Participants who could become pregnant or who have partners who could become pregnant must either commit to continued abstinence from heterosexual intercourse or begin using effective birth control during the study and for 30 days after stopping

treatment. If you are a woman who could become pregnant, you will receive counseling about committing to abstinence or using TWO types of effective barrier birth control, one highly effective method and one additional method. If you are a man who could father a child, you will receive counseling about committing to abstinence or using a condom and the risks of sEphB4-HSA on a fetus. Ask your doctor or study nurse for more information about types of effective barrier birth control and preventing pregnancy. Tell the study doctor immediately if you or your partner becomes pregnant while taking part in this study. We will follow you during the pregnancy and after giving birth for potential side effects.

Types of effective birth control are:

- Highly effective methods:
 - Intrauterine device (IUD)
 - Hormonal (birth control pills, injections, implants)
 - Tubal ligation
 - Partner's vasectomy
- Additional effective methods:
 - Male condom
 - Diaphragm
 - Cervical Cap

Unknown Risks: You may have side effects of sEphB4-HSA that are not yet known. These side effects may be a minor inconvenience. Or, they could be severe enough to be life-threatening or cause death. You will be watched closely for side effects. The drug will be stopped if unwanted or serious side effects develop. There may also be other unknown effects during the time you take part in the study or after the study is complete.

For more information about risks and side effects, ask your doctor.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

WHAT POSSIBLE BENEFITS CAN I EXPECT FROM TAKING PART IN THIS STUDY?

This study has only a small chance of helping you because we do not know if the study drug sEphB4-HSA is effective. This study may help researchers learn things that may help other people in the future.

CAN I STOP TAKING PART IN THIS STUDY?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If you become pregnant or breastfeed
- If new information becomes available

- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

WHAT ARE MY RIGHTS IN THIS STUDY?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights as a research participant, contact the _____ (insert name of center) Institutional Review Board (which is a group of people who review the research to protect your rights) at _____ (insert telephone number). A non-physician whom you may call for information about the consent process, research subject's studies. (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

The study drug sEphB4-HSA will be supplied by the drug company at no charge while you take part in this study. The cost of getting the study drug sEphB4-HSA ready and giving it to you is also provided at no charge. It is possible that the study drug sEphB4-HSA may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs caring for your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will be paid \$50 for the following visits: eligibility, screening, on-study visits 1-12, and end of treatment. You will be paid up to \$600 for on-study visits. You will also be paid \$25 for each post-treatment evaluation (up to 4 visits) for your participation in this study. You will be paid immediately after each cycle or visit via prepaid credit card.

We will not pay you for any discovery, invention, development, or method of treatment that may result from you taking part in this research.

You can visit the NCI's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage> for more information on clinical trials and insurance coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" brochure from this Web site. You can also ask for a free copy by calling NCI at 1-800-4-CANCER (1-800-422-6237).

[Note to site: Modify this section as needed for local reimbursement methods]

WHAT HAPPENS IF I AM INJURED OR HURT BECAUSE I TOOK PART IN THIS STUDY?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

WHO WILL SEE MY MEDICAL INFORMATION?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The AIDS Malignancy Consortium (AMC)
- The National Cancer Institute (NCI)
- VasGene, the drug company supporting the study drug sEphB4-HSA
- The Institutional Review Board (IRB) is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration (FDA) in the U.S.

WHERE CAN I GET MORE INFORMATION?

You may visit the NCI Web site at <http://cancer.gov/> for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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 can search this Web site at any time.

WHO CAN ANSWER MY QUESTIONS ABOUT THIS STUDY?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ (*study investigator's name*) at _____ (*insert telephone number*).

For questions about the study or a research-related injury, you may also contact the research coordinator _____ (*study coordinator's name*) at _____ (*insert telephone number*).

OPTIONAL SAMPLE COLLECTIONS FOR LABORATORY STUDIES AND DONATION OF LEFTOVER TISSUE SAMPLES TO THE AIDS AND CANCER SPECIMEN RESOURCE (ACSR)

This section is about optional studies you can choose to take part in

Researchers are trying to learn more about cancer, HIV/AIDS, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems. Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part in this study, the study doctor for the main study would like to collect unused blood and biopsy tissue left over after the study is done. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking.” The Biobank is being run by the **AIDS and Cancer Specimen Resource** and is supported by the National Cancer Institute.

What is involved?

If you agree to take part, here is what will happen next:

- 1) Your sample and some related health information will be stored in the ACSR Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record may be updated after the study is over.
- 2) Qualified researchers can submit a request to use the materials stored in the ACSR. A science committee at the ACSR will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
- 3) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
- 4) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

What are the possible risks?

- 1) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
- 2) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
- 3) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information

about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

How will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

- 1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
- 2) The list that links the unique code to your name will be kept separate from your sample and health information. The ACSR and AMC staff with access to the list must sign an agreement to keep your identity confidential.
- 3) Researchers to whom the ACSR and the AMC send your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
- 4) Information that identifies you will not be given to anyone, unless required by law.
- 5) If research results are published, your name and other personal information will not be used.

What are the possible benefits?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments?

There are no additional costs to you or your insurance for these optional studies. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, (*insert name of study doctor for main trial*) at _____ (*insert telephone number of study doctor for main trial*) who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

What if I have more questions?

If you have questions about the use of your samples for research, contact the study doctor, _____, (*insert name of study doctor for main trial*), at _____ (*insert telephone number of study doctor for main trial*).

Please circle your answer to show whether or not you would like to take part in each option:

Samples for future research studies:

My samples and related information may be donated to ACSR Biobank for use in future health research.

YES

NO

I agree to have my samples undergo genetic testing to learn about, prevent, diagnose, or treat HIV-related diseases and cancer.

YES

NO

This is the end of the section about optional studies.

MY SIGNATURE AGREEING TO TAKE PART IN THE MAIN STUDY

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes'.

Participant's signature: _____

Date of signature: _____

Signature of person(s) conducting the informed consent discussion: _____

Date of signature: _____

ATTACHMENT 1: AMC CERTIFICATE OF CONFIDENTIALITY STATEMENT

The NIH has given the AMC a Certificate of Confidentiality. The Certificate does not mean that the NIH or the U.S. Government recommend that you take part in this study. This Certificate helps us keep your health information private.

Your records for this study will have information that may identify you. This Certificate lets us turn down legal demands for your study records. We can use the Certificate to turn down demands for records from a U.S. court. The Certificate can be used in any federal, state, or local legal matters. We will use the Certificate to turn down any demands for your study records. The cases where we cannot use the Certificate are explained below.

We cannot use the Certificate to turn down a demand from the U.S. Government for study records. This applies to audits or reviews of the AMC. This also applies to study records that we have to report to the FDA.

The Certificate does not stop you or your family members from sharing your health information. It does not stop you from talking about taking part in this study. You may give written permission for an insurer, employer, or other person to get copies of your study records. If you give permission, we cannot use the Certificate to say no to a request for your study records.