S1702 Research Study Informed Consent Document

Study Title for Study Participants: Study of Isatuximab (SAR650984) in Patients with Previously Treated Amyloidosis

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: **S1702**, A Phase II Study of Isatuximab (SAR650984) (NSC-795145) for Patients with Previously Treated AL Amyloidosis

What is the usual approach to my Amyloidosis?

You are being asked to take part in this study because you have amyloid light chain (AL) amyloidosis which has gotten worse or has recurred. People who are not in a study are usually treated with either supportive care drugs (to treat the symptoms of amyloidosis affecting the heart, kidney, liver, gastrointestinal system, nerves, and soft tissue), drugs that try to slow the progress of amyloidosis including steroids, chemotherapy, drugs that can trigger cancer cell death, or drugs that affect how the immune system work. Sometimes, combinations of these treatments are used and your doctor can explain which may be best for you. These treatments can reduce symptoms and may slow or stop the systematic light chain (AL) amyloidosis 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 your disease.

Why is this study being done?

The purpose of this study is to test for any good and bad effects of the study drug called isatuximab. Isatuximab may or may not improve your AL amyloidosis but it could also cause side effects. Isatuximab is not approved by the Food and Drug Administration (FDA). Isatuximab has been shown to have good effects in some patients with recurring multiple myeloma. For this reason, the researchers think that isatuximab may also help patients whose amyloidosis has recurred or gotten worse. To decide if the study treatment is better than the usual approach, the study doctors will be looking to see if the study treatment increases the number of patients whose disease responds to treatment by at least 30 percent.

There will be about 39 people taking part in this study.

What are the study groups?

All study participants will receive the same study drug (intervention).

You will receive up to 24 cycles of the study drug, isatuximab, as an outpatient (meaning you will not be admitted to the hospital to receive study drug). On the days that you receive study drug, you will receive medication prior to receiving the study drug to help prevent an adverse reaction to the study drug. One cycle of study drug = 28 days. During the first cycle (or 28 days), you will receive isatuximab on Day 1, 8, 15 and 22 by intravenous (IV) infusion (into your vein). For all other cycles (Cycle 2, up to Cycle 24), you will receive isatuximab on Days 1 and 15.

After you receive the study drug, you will need someone to drive you home from the outpatient clinic. Because the study drug can affect blood typing test results, you will also be given a "type and screen" information card to carry. You should keep this information card with you at all times.

How long will I be in this study?

You will receive the study drug for up to two years, or until your disease gets worse, you have unacceptable side effects from the study drug, or you or your investigator choose to stop the therapy for another reason. After you finish taking the study drug, your doctor will continue to watch you for side effects and follow your condition. For this reason, you will have a study visit every 6 months for 2 more years or until your disease get worse. After your disease gets worse, your doctor will continue to watch you as is appropriate standard of care for your disease.

What extra tests and procedures will I have if I take part in this study?

Thera are no extra tests or procedures (outside the normal standard of care) that are involved.

What possible risks can I expect from taking part in this study?

The drug 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(s)/study approach. 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 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 drug to try to reduce side effects.**

The tables below show 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. If important new side effects are found, the study doctor will discuss these with you.

COMMON, SOME MAY BE SERIOUS In 100 people receiving isatuximab, more than 20 and up to 100 may have:

• **Nausea, Diarrhea, Vomiting**
• **Cough**
• **Back pain**
• **Tiredness**
• **Chills, Fever**
• **Reaction that can occur during or following infusion of the drug. The reaction may include fever, chills, rash, low blood pressure, and difficulty breathing.**
• **Infection of the upper respiratory tract (nose, sinuses, throat, wind pipe, and voice box)**
• **Severe illness in which the bloodstream is overwhelmed by bacteria**
• **Changes in laboratory tests values (blood counts) including:**
  • **Decreased number of white blood cells that help fight infection**
  • **Decreased number of platelets in the blood that may cause slow blood clotting or bruising**
  • **Increased levels of liver enzymes or liver pigment, which may be a sign of liver problems**
  • **Increased blood level of creatinine (a substance normally eliminated by the kidneys into the urine)**
  • **Increased blood level of calcium**

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving isatuximab, from 4 to 20 may have:

- **Pain, Stomach Pain, Eye Pain, Pelvic Pain, Muscle Pain, Bone Pain, Chest Pain**
- **Headache, Dizziness, Weakness, Lack of Energy**
- **Lightheaded, Shortness of Breath (hyperventilation)**
- **Constipation**
- **Decreased appetite (not hungry)**
- **Difficulty seeing**
- **Swelling of the face or throat**
- **Fear of light**
- **Low blood pressure**
- **Increased blood thickness that may cause bleeding from mucous membranes**
- **Abnormally fast irregular heartbeat involving the upper chambers of the heart (atria)**
- **Collection of signs and symptoms that indicate sudden heart disease in which the heart does not get enough oxygen. Sudden symptoms such as chest pain, shortness of breath, or fainting could indicate heart disease and should be reported right away. Signs such as abnormal EKG and blood tests can confirm damage to the heart.**
- **Bronchitis (Swelling of the air passage between the mouth/nose and the lungs) which may cause difficulty breathing;**
- **Sudden constriction of the small airways of the lung that can cause wheezing and shortness of breath**
- **Stopping of breathing (apnea)**
- **Partial lung collapse**
- **Flu (including body aches, fever, chills, tiredness, loss of appetite, cough)**
- **Fever associated with dangerously low levels of a type of white blood cell (neutrophils)**
- **Lung infection; Infection (pneumonia) or Inflammation of the lungs that may cause difficulty breathing and can be life threatening.**
- **Infection in the stomach, urinary tract, upper respiratory tract (nose, sinuses, throat, wind pipe, and voice box); Middle ear infection**
- **Uncontrolled contractions of the muscles of the vocal cords**
- **Rash; Shingles; Chickenpox**
- **Broken hip; broken arm; joint injury**
- **Fall; Bone break or fracture due to fall**
- **Bleeding during an operation**
- **Tumor lysis syndrome- Group of signs and symptoms due to rapid breakdown of tumor that can occur after treatment of cancer has started that causes increased levels of blood potassium, uric acid, and phosphate, decreased levels of blood calcium, and kidney failure**
- **Convulsion or seizure**
- **Changes in laboratory values, including: Increased blood level of calcium, Excess levels of a liver pigment (bilirubin) in the blood, which is often a sign of liver problems**
- **Disease getting worse (decreased performance status)**

RARE, AND SERIOUS In 100 people receiving isatuximab, 3 or fewer may have:
• **Heart and lungs stops working** • **Infection of the lung (pneumonia), inflammation of the lungs that may cause difficulty breathing and can be life threatening, or lung infection that develops after breathing solids or liquids into the lungs** • **Build-up of a large amount of fluid between the layers of tissue that line the lungs and chest cavity, or Failure of the lungs (respiratory system) to perform its function of taking in oxygen and giving off carbon dioxide** • **Blood clot in the lungs** • **Coughing up blood** • **Inflammation (due to infection) of the artery to your heart; enlargement or bulge in the aorta (main artery); or weakness of the heart due to emotional or physical stress** • **Vein compression that may result in swelling of the legs** • **Severe and fast rise in blood pressure** • **Blockage of small intestine, bleeding of the belly, or abnormally slow bowel contraction** • **Collapse or tunneling (fold over) of the intestine onto itself** • **Blockage of the stomach** • **Inflammation of the colon due to infection** • **Stomach pain and or inflammation due to virus** • **Swelling of the tongue** • **Medical device not working properly** • **Disease getting worse** • **Difference in normal walking** • **Severe allergic reaction** • **Severe illness in which the bloodstream is overwhelmed by bacteria. This widespread infection may cause organ failure and dangerously low blood pressure. May be life-threatening.** • **Infection and inflammation of the lining of the abdominal cavity** • **Infection or inflammation (swelling and redness) of the connective tissue surrounding the brain and spinal cord** • **Compression of the spinal cord** • **Stroke that comes and goes quickly (a mini stroke) with no lasting effects. They can be a warning of future stroke.** • **Bleeding in the brain** • **Flu** • **Bone fracture due to weakening of the bones** • **Skin Cancer; Cancer of the blood and bone marrow; Cancer of the mouth;** • **Sudden decrease of kidney function; Kidney failure** • **Rapid swelling of the skin, usually around the lips, eyes, tongue, hands or feet**

You should avoid green tea and green tea extracts as they contain a component that can affect the way your body responds to the study drug.

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.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The study drug used in this study could be very damaging to an unborn baby. If you are a female that is able to become pregnant, you must agree not to become pregnant while taking the study drug and for at least 12 weeks after you receive the last dose of the study drug. If you are a female that is able to become pregnant, you must also agree to have a pregnancy test prior to each cycle of treatment. Check with your doctor about what type of birth control methods to use and how long to use them. If your uterus and/or both ovaries have not been removed, or if you have had at least one menstrual period in the past 24 months and/or your menses stopped due to treatment of your disease, you will be considered a female that is able to become pregnant. If you are a male, you must agree to use an approved form of birth control while on study and at least 12 weeks after you receive the last dose of the study drug.

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/study approach 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 new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or U.S. Food and Drug Administration (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 while in this study, call the _____ *(insert name of center)* **Institutional Review Board at** _____ *(insert telephone number). (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 isatuximab will be supplied at no charge while you take part in this study. It is possible that the isatuximab 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 of treating your disease 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. The cost of getting the isatuximab ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. 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 not be paid for taking part in this study.

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. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.

Some of these organizations are:

- The study sponsor (SWOG) and any drug company supporting the study (Sanofi U.S. Services)

- 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 and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

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 _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION:

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

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with amyloidosis in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Please circle your answer:

FUTURE CONTACT

I agree to allow my study doctor, or someone approved by my study doctor, to contact me regarding future research involving my participation in this study.

YES NO

Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies

Researchers are trying to learn more about amyloidosis, diabetes, 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, a bone marrow aspirate and biopsy samples and a blood sample will be collected as described below. The researchers ask your permission to store and use your samples and related health information (for example, your response to 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 SWOG and supported by the National Cancer Institute.

WHAT IS INVOLVED?

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

1) At the time of normal standard of care procedures, an additional 3 teaspoons of blood will be collected from a vein in your arm, about 1 teaspoon of bone marrow aspirate and about 2 cm of bone marrow biopsy will be collected. For the bone marrow aspiration/biopsy, a needle is inserted into the bone, usually in the hip or spine, and the soft tissue of the middle of the bone is removed. These extra samples will be collected at the same time of standard of care procedures occurring within 35 days prior to the start of treatment with the study drug. Your sample and some related health information may be stored in the 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 will be updated from time to time.
2) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, 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) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) The most common risks related to bone marrow aspirate and biopsy are excessive bleeding, infection, long-lasting discomfort at the biopsy site, penetration of the breastbone that may cause heart or lung problems (during sternal aspiration).
3) 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.
4) 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.
5) 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. Any Biobank and SWOG staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom SWOG sends 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 costs to you or your insurance. 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 will either be destroyed or returned to your doctor (whichever your study doctor requests). 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:

Please circle your answer:

SAMPLES FOR FUTURE RESEARCH STUDIES:

My bone marrow biopsy samples and related information may be kept in a Biobank for use in future health research.

YES NO

My bone marrow aspirate samples and related information may be kept in a Biobank for use in future health research.

YES NO

My blood samples and related information may be kept in a Biobank for use in future health research.

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_____