Informed Consent to Participate in Research

BMT CTN 2002

A PHASE 3, RANDOMIZED, OPEN-LABEL, MULTICENTER STUDY, TO COMPARE T-GUARD TO RUXOLITINIB FOR THE TREATMENT OF PATIENTS WITH GRADE III OR IV STEROID-REFRACTORY ACUTE GRAFT-VERSUS-HOST DISEASE (SR-AGVHD)

Your Name: _____

Principal Investigator: _____

[Insert local PI information]

Sponsor: This study is sponsored by Xenikos, BV and the National Institutes of Health, through the Blood and Marrow Transplant Clinical Trials Network

<*US country specific language, please delete for other countries*>

The ethics of this study have been reviewed and approved by the NMDP IRB.

<*Europe country specific language, please delete for other countries*>

The ethics of this study have been reviewed and approved by the EC in your country.

Your study doctor or nurse will review this **Consent Form** with you, including:

- ✓ The purpose of the research
- ✓ Possible risks and benefits
- ✓ Other options available to you
- ✓ Your rights if you join the study

1. Study Overview

We invite you to join this clinical trial, also known as a research study. You are being asked to join because:

- You have acute graft-versus-host disease (aGVHD)
- Your aGVHD symptoms did not get better with steroids (steroid-refractory)

We're doing this study because we want to see how well a new medicine, T-Guard, works compared to another medicine called ruxolitinib.

In a previous clinical trial, ruxolitinib improved aGVHD for about half of patients. However, most patients still had aGVHD symptoms after a month of treatment. Ruxolitinib also has side effects and doctors don't know how long patients should take it. We are testing whether T-Guard works better and has fewer side effects.

This study will include 246 people at about 75 hospitals across the USA and Europe and will last about 3 years. If you join, you will:

- Be in the study for up to 180 days, and contacted for follow-up after that
- Get either T-Guard or ruxolitinib to treat your aGVHD. If your doctor thinks it's best for your health, you will also keep taking your steroid medicine.
- Give blood and urine samples to see how your body responds to the treatment
- Take surveys about your quality of life or ability to complete daily tasks

Some possible risks and benefits of joining the study include:

> **Possible Risks:** T-Guard or ruxolitinib may not help your aGVHD. You may have side effects during the study. Specific side effects depend on which medicine you get and can range from mild to severe. The study team will watch you carefully for any side effects and will do everything they can to keep you safe and treat any side effects.
>
> **Possible Benefits:** T-Guard or ruxolitinib may help your aGVHD. Doctors may learn more about T-Guard and ruxolitinib to treat future patients with aGVHD that doesn't get better with steroids.

If you do **not** join the study, your doctor will talk to you about other treatment options.

<*US country specific language, please delete for other countries*>

Ruxolitinib is the only drug approved by the FDA for treating aGVHD that does not get better

with steroids. You may have the option to receive ruxolitinib without joining the study.

<*Europe country specific language, please delete for other countries*>

In Europe there is not an approved drug to treat aGVHD that does not get better with steroids. Your doctor will talk to you about the best options to treat you.

Key points:

- Being in this research study is your choice.
- You may or may not benefit from being in the study. Knowledge gained from this study may help others.
- If you join the study, you can leave the study at any time. If you decide to leave the study, it will not affect your care at [name of facility or institution].
- Ask the study staff questions about anything you do not understand, or if you would like more information. You can ask questions now or at any time.
- Take time to talk about the study with your doctor, study staff, and your family and friends. It is **your** choice to be in the study. If you decide to join, please sign the end of this Consent Form. You'll get a copy to keep.

2. Study Purpose

We're doing this study to see how T-Guard works compared to ruxolitinib to treat aGVHD that doesn't get better with steroids. We want to know if T-Guard and ruxolitinib therapy will make your aGVHD go away completely after 28 days.

Even though doctors have learned a lot about how the immune system reacts to a blood or marrow transplant (BMT), aGVHD is a common and serious side effect. Doctors and researchers want to find a good treatment for aGVHD when it doesn't get better with steroids.

This study is designed to see the benefits and risks of T-Guard. T-Guard has not been approved by the FDA, European Medicines Agency (EMA), or other regulatory authorities. T-Guard, as of November 2020, has been given to 44 patients with aGVHD that did not respond to steroids. T-Guard improved aGVHD in over half of those patients.

This research study is registered with the FDA and EMA. Both will monitor the research study.

3. Study Treatment and Tests

Once you agree to be in the study, you will need to have several tests to see if you meet the study requirements. Most of these check-ups and tests are already part of your regular care and will be done even if you do not join the study. The tests include:

- Complete aGVHD and medical history evaluation
- Draw blood (about 15 mL or 3 teaspoons *[insert volume according to local standard]*) to test:
    - The number of different blood cells you have (cell counts)
    - How well your liver and kidneys work
    - If there is any damage to your blood and vessels
- Pregnancy test (if you could be pregnant)

Before Your Treatment

If you meet the study requirements, a computer will assign you to get either T-Guard or ruxolitinib. The computer assigns you by chance, like flipping a coin or drawing a name out of a hat. This is called **randomization**. Neither you nor your study doctor will have any control over which treatment group you're assigned to. You'll have an equal chance of being assigned to either group.

Before you start your treatment, we will do several tests to check your health. These tests will include:

- Physical exam, including a Performance Score. A Performance Score is when your doctor will see how well you can do certain activities like going to work and caring for yourself.
- Complete aGVHD evaluation
- Draw blood (about 15 mL or 3 teaspoons *[insert volume according to local standard]*) to test:
    - The number of different blood cells you have (cell counts)
    - How well your liver works
    - If you have cytomegalovirus (CMV) or Epstein-Barr virus (EBV). CMV and EBV may not cause symptoms before transplant but can be serious after getting a transplant.
- Research blood samples to see:
    - How your immune cells respond to the treatment (about 5 mL or 1 teaspoon will be drawn) if you are randomized to receive T-Guard
    - How your blood cells respond to the treatment (about 30 mL or 2 tablespoons will be drawn)

  - How your immune system recovers (about 10 mL or 2 teaspoons will be drawn)
  - Whether changes in your blood cells (biomarkers) show if the treatment works for you (about 5 mL or 1 teaspoon will be drawn)
- Research urine sample to see whether changes in your urine (biomarkers) show if the treatment works for you (about 6 mL or 1 teaspoon will be collected)
- A series of questionnaires to see how the disease and treatment has affected your quality of life. They will take about 20 to 30 minutes to complete. If you use reading glasses, bring them to your appointments.

During the Study

During the study, we will do regular tests to check your health during and after you get treatment. Many tests will be done once a week for about 8 weeks after you start study treatment. Some tests will happen less often. We'll look at:

- Your aGVHD
- For signs of chronic graft-versus-host disease (cGVHD)
- Your Performance Score
- Your blood pressure
- Draw blood (about 15 mL or 3 teaspoons *[insert volume according to local standard]*) to test:
  - How many different blood cells you have (cell counts)
  - How well your liver and kidneys work
  - If there is damage to your blood and vessels
  - If you have cytomegalovirus (CMV) or Epstein-Barr virus (EBV).
- Research blood samples to see:
  - How your immune cells respond to the treatment (about 5 mL or 1 teaspoon will be drawn) if you are randomized to receive T-Guard
  - How your blood cells respond to the treatment (about 30 mL or 2 tablespoons will be drawn)
  - How your immune system recovers (about 10 mL or 2 teaspoons will be drawn)
  - Whether changes in your blood cells (biomarkers) show if the treatment works for you (about 5 mL or 1 teaspoon will be drawn)
- Research urine sample to see whether changes in your urine (biomarkers) show if the treatment works for you (about 6 mL or 1 teaspoon will be collected)
- Any side effects you may have and medications you may be taking
- A series of questionnaires to see how the disease and treatment has affected your quality of life. They will take about 20 to 30 minutes to complete. If you use reading glasses,

bring them to your appointments.

If you're randomized to T-Guard, you can expect to:

- Stay in the hospital for at least 1 week
- Get T-Guard through an intravenous (IV) infusion every 2 days for a total of 4 doses. Each infusion takes 4 hours.
- Get medicine to prevent allergic reactions before each dose
- Have your temperature, heart rate, breathing rate, and blood pressure checked during and after each infusion
- Draw blood before, right after, and the day after each dose of T-Guard (about 5 mL or 1 teaspoon will be drawn each time; with a total maximum of 25 mL or 5 teaspoons on the day of infusion) to see:
    - How much T-Guard is in your blood
    - The amount of proteins in your blood that may change your immune response

When you finish T-Guard treatment, you'll visit the clinic at least 1 time each week for 7 weeks. Then, you'll visit the clinic on days 70 and 90, and 180 after treatment. Your doctor may want to see you more often.

If you're randomized to ruxolitinib, you can expect:

- You'll take ruxolitinib, which is in pill form, 2 times each day by mouth for at least 56 days.
- You'll visit the clinic at least 1 time each week for 8 weeks when you start treatment. Then, you'll visit the clinic on days 70, 90, and 180 after treatment. Your doctor may want to see you more often.

Tables 1 and 2 show all the tests you can expect to get for each treatment. The numbers for each column are the number of days after your first study treatment.

Table 1. Schedule of Study Tests for T-Guard

Test	Prior to Randomization	Day of Randomization and Prior to Treatment	First Infusion	Second Infusion	Third Infusion	Fourth Infusion	Follow-up (# days after randomization)									
			0	2	4	6	14	21	28	35	42	49	56	70	90	180
Acute GVHD evaluation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood pressure			X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood tests to see:																
• Your protein levels	X		X	X	X	X			X				X		X	X
• How well your liver works	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
• How well your kidneys work	X					X	X	X	X							
• If there is damage to your blood and vessels	X					X	X	X	X							
• How much enzyme is in your muscles	X															
• How many different cells are in your blood	X	X	X	X	X	X	X	X	X				X		X	X
• If you have EBV or CMV		X				X	X	X	X	X	X	X	X			X
• How well your immune cells work		X					X		X				X			X
• How many antibodies you have		X					X		X				X			X
• How your body is responding to the drug		X				X	X		X							
• How the GVHD is responding to the drug		X				X	X		X						X	X
• How much T-Guard is in your blood			X	X	X	X										
Chronic GVHD evaluation									X				X		X	X
Health history	X															
Performance Score (How well you can do daily activities)		X							X				X		X	X
Physical exam		X	X	X	X	X										
Pregnancy test (if applicable)	X															
Quality of life questions		X							X						X	X
Urine sample for GVHD biomarkers		X				X	X		X							

Table 2. Schedule of Study Tests for Ruxolitinib

Test	Prior to Randomization	Day of Randomization and Prior to Treatment	Treatment and Follow-up (# days after randomization)											
			0	6	14	21	28	35	42	49	56	70	90	180
Acute GVHD evaluation	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Blood pressure			X	X	X	X	X	X	X	X	X	X	X	X
Blood tests to see:														
• Your protein levels	X		X	X			X				X		X	X
• How well your liver works	X	X	X	X	X	X	X	X	X	X	X	X	X	X
• How well your kidneys work	X			X	X	X	X							
• If there is damage to your blood and vessels	X			X	X	X	X							
• How much enzyme is in your muscles	X													
• How many different cells are in your blood	X	X	X	X	X	X	X				X		X	X
• If you have EBV or CMV		X		X	X	X	X	X	X	X	X			X
• How well your immune cells work		X			X		X				X			X
• How many antibodies you have		X			X		X				X			X
• How the GVHD is responding to the drug		X		X	X		X						X	X
Chronic GVHD evaluation							X				X		X	X
Health history	X													
Performance Score (how well you can do daily activities)		X					X				X		X	X
Physical exam		X												
Pregnancy test (if applicable)	X													
Quality of life questions		X					X						X	X
Urine sample for GVHD biomarkers		X		X	X		X							

4. Risks and Benefits

Possible Benefits

T-Guard or ruxolitinib may help your aGVHD get better. Doctors may learn more about T-Guard and ruxolitinib to treat future patients with aGVHD that doesn't get better with steroids.

Possible Risks

T-Guard or ruxolitinib may **not** help your aGVHD get better. You may have side effects that range from mild to severe (including death). Your health care team may give you medicine to help with certain side effects, like an upset stomach.

Your doctor will watch you carefully for any side effects. The study team will do everything they can to keep you safe and to treat any side effects. Tell your doctor about any side effects you have.

A. Risks of T-Guard

As of November 13, 2020, 44 patients have received T-Guard through their participation in a clinical trial or special access program for the treatment of aGVHD that did not respond to steroids (43 patients) or for the treatment of Systemic Sclerosis (1 patient). The side effects, as seen in aGVHD patients that used T-Guard as 2nd line treatment, are shown in the table below. Several of these side effects are common in people with aGVHD. T-Guard might increase the likelihood that (some of) these side effects develop. Of the patients that received T-Guard, some died within 30 days of getting their first dose of T-Guard. Although it is possible T-Guard contributed to these deaths, these patients were also very ill with other complications when they started treatment. The eligibility criteria to be allowed to be part of this study help to reduce the risks for patients. Your study doctor can provide more details on how we will be monitoring your safety.

Table 3. Risks and Side Effects of T-Guard

Likely (Seen in more than 20% of patients)	**Less Likely** (Seen in 10% to 20% of patients)
• Fever • High blood sugar • High protein or enzyme levels in your blood, which could be a sign of liver damage • Infections, which could be mild to moderate (for instance in the lungs, mouth, eyes, skin, urinary tract) which may or may not require treatment or could be severe and lead to death • Low platelet counts, which may cause bruising or bleeding • Low protein, calcium, magnesium, or phosphate levels in your blood • Muscle weakness • Swollen arms, legs or other body parts • Blood vessels leaking fluid to your body tissues, which may result in swelling	• Abdominal pain • Bleeding in your stomach or intestines • Changes to the acid level of your blood • Chronic GVHD • Confused thinking • Cough • Damaged red blood cells • Difficult breathing • Fatigue or tiredness • Headache • Hemorrhoids or piles • High heart rate and heart rhythm changes • High potassium or sodium levels in your blood • Indigestion (pain in the stomach after eating) • Kidney reduced functioning or failure • Low blood pressure • Low potassium or sodium levels in your blood • Low red blood cell counts • Low white blood cell count, which can raise your risk of infection • Nausea • Pain, bruising or swelling where you got the infusion • Pain in arms, hands, legs, or feet • Thrombotic Microangiopathy (TMA): Developing GVHD increases your risk for TMA. TMA can lead to low blood counts, organ failure, such as kidney failure, and even death. It is possible that T-Guard may further increase your risk of TMA. We will monitor you closely for signs of TMA and we will not continue treatment with T-Guard if you develop TMA.

Potential serious risks in medicines like T-Guard

T-Guard belongs to a family of drugs (antibodies that are connected to a toxin), and some of the drugs in this family have certain side effects. When these side effects occur, they may have serious consequences. These side effects are:

- Swelling of the muscles causing muscle pain and weakness
- Life-threatening allergic reactions (anaphylaxis) to the drug, which may cause trouble breathing and death
- Cytokine release syndrome, which can cause fever, nausea, headache, rash, fast heartbeat, low blood pressure, and trouble breathing

Reproductive and Breastfeeding Risks with T-Guard

T-Guard **may or may not** affect your ability to have children. We also don't know how it affects unborn babies. Because of this, it is important that you are not pregnant or breastfeeding and that you (or your partner) do not become pregnant while you're in this study.

If you are sexually active, you will need to use birth control. Talk with your doctor about ways to prevent pregnancy. If you can become pregnant, you must use birth control until 30 days after your last infusion of T-Guard. If your partner can become pregnant, you must use birth control from the start of your treatment until 65 days after your last infusion of T-Guard.

Tell your doctor right away if you or your partner becomes pregnant during the study. Your doctor will talk with you about the risks to your unborn child and your options. If you are pregnant, you will be asked to stop study treatment.

B. Risks of Ruxolitinib

The table below shows side effects seen in people who have received ruxolitinib.

Table 4. Risks and Side Effects of Ruxolitinib

Likely (Seen in more than 20% of patients)	**Less Likely** (Seen in 10% to 20% of patients)	**Rare, but Serious** (Expected to happen in 2% or fewer patients)
• High cholesterol • Increased enzyme levels in your blood, which could be a sign of liver damage • Low platelet levels, which may cause bruising or bleeding • Low red blood cell counts	• Diarrhea, constipation, nausea, passing gas • Dizziness • Headache • High blood pressure • High triglyceride levels in your blood • Infection, which may cause fever and chills • Low white blood cell count, which can raise your risk of infection • Muscle spasms • Problems sleeping • Trouble breathing • Weight gain	• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Brain swelling that can cause confusion, weakness, trouble speaking, sadness or personality changes, trouble with memory, balance problems, and/or changes in vision • Skin cancers

Reproductive and Breastfeeding Risks with Ruxolitinib

Although the FDA allows for ruxolitinib to be used for someone who is pregnant if the potential benefits to the parent outweigh the potential risks to the unborn child, these risks are not fully known. In animal studies, pregnant animals were given this medication and had some babies born with problems. It is important that you are not pregnant or breastfeeding and that you (or your partner) do not become pregnant while you're in this study.

If you are sexually active, you will need to use birth control. Talk with your doctor about ways to prevent pregnancy. If you can become pregnant, you must use birth control until 30 days after your last dose of ruxolitinib. If your partner can become pregnant, you must use birth control from the start of your treatment until 65 days after your last dose of ruxolitinib.

Tell your doctor right away if you or your partner becomes pregnant during the study. Your doctor will talk with you about the risks to your unborn child and your options. If you are pregnant, you may be asked to stop study treatment.

C. Other Risks

Infections

Because your immune system will be weak, you have a higher risk for infections, which can be fatal. You'll get medicines to help your body prevent infection, but you'll still be watched carefully for any sign of infection. Tell your doctors right away if you get a fever, chills, cough or any other new symptoms. They may be a sign of an infection.

Other Treatments or Medicines

Some medicines react with each other, so it's important to tell the study doctor or staff about any other drugs, treatments, or medicines you're taking. This includes non-prescription or over-the-counter medicines, vitamins, and herbal treatments.

It's also important that you tell the study staff about any changes to your medicines while you're in the study.

Blood Draws

There are no major risks associated with drawing blood. Having your blood drawn can be uncomfortable and can sometimes cause a bruise. In rare cases, a blood draw can cause fainting. Only trained people will draw your blood.

Surveys

There are very few risks with taking the study surveys. Some of the questions or topics may upset you. If you are sad or upset, or if some of the survey questions or topics upset you, it is important to tell your doctor and care team. Your doctors can connect you with a counselor or trained support specialist if you want one.

Unforeseen Risks

There may be some unknown or unanticipated side effects from being in this study. Other new risks might come up at any time during the study. These risks might be different from what is listed in this Consent Form.

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

5. Your Rights to Withdraw, Ask Questions, and Seek Other Treatment

Being in this study is your choice. You can choose **not** to be in this study or leave this study at any time. If you choose to not join or leave this study, it won't affect your regular medical care in any way. If the treatment does not work, you can still receive other treatment options available.

You have the right to ask questions about the study at any time. If you have questions about your rights as a participant or you want to leave the study, please contact:

[Insert contact details]

If you want to talk with someone not directly involved in the study, or have any complaints or questions about your rights as a research participant, you may contact:

[Insert contact details]

If you choose not to join, other options are available. Your study doctor will talk with you about your options. If you decide not to join this study, your medical care will not be affected in any way.

Every treatment option has benefits and risks. Talk with your doctor about your choices before you decide if you will be in this study.

6. New Information Available During the Study

During this study, the study doctors may learn new information about T-Guard, ruxolitinib or the risks and benefits of taking part in the study. If they learn new information, they'll tell you as soon as it's available.

The new information may mean that you can no longer participate in the study, or you may not want to continue. If this happens, the study doctor will stop your participation and offer you all available care to meet your health care needs.

7. Privacy, Confidentiality, and Use of Information

<*UK country specific language, please delete for other countries*>

Xenikos, BV (Xenikos) is the sponsor for this study taking place in the United Kingdom and elsewhere. Xenikos will be using information from you in order to undertake this study and will act

as the data controller for this study. This means that Xenikos will be responsible for looking after your information and using it properly. [*<Optional if applicable>* Xenikos has appointed [CRO] as its 'representative' to fulfil its obligations under this law.] Xenikos will keep identifiable information about you for 25 years after the study has finished. The information may be stored for longer, for example, when used in applications for approval to market a medicine.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

We use personally-identifiable information to conduct research to improve health and care. As a pharmaceutical company we have a legitimate interest in using information relating to your health and care for research studies, when you agree to take part in a research study. This means that we will use your data, collected in the course of a research study, in the ways needed to conduct and analyse the research study.

Your personal information may be shared with:

- Xenikos and its present or future affiliates,
- Research partners/service providers (such as laboratories conducting tests on behalf of Xenikos) and authorized representatives of Xenikos,
- Study monitors appointed by Xenikos or Xenikos' service providers to check how the study is going,
- Auditors/inspectors appointed by Xenikos or Xenikos' service providers or by health and regulatory authorities to check that the study is being run properly,
- Relevant health and regulatory authorities such the Food and Drug Administration (FDA) in the United States of America and the European Medicines Agency (EMA).

Recipients of your information may be in countries that do not provide the same standard of legal protection for your information as in the United Kingdom, raising the risk that you will not be able to enforce the above rights and recipient organisations may not be legally required to fully secure your data. Xenikos is taking appropriate safeguards to make sure that your personal information is protected. These include implementing special contract clauses, known as Standard Contractual Clauses, which protect transfers of personal information between companies in Xenikos, which can be provided on request. Xenikos is implementing similar appropriate safeguards with third party service providers and partners, and further details can be provided upon request. If you wish to obtain a copy of the Standard Data Protection Clauses, you should firstly contact your study doctor

who will be able to direct your query where appropriate to staff responsible for data protection at the [Sponsor] or site, including the site Data Protection Officer

[NHS/other site] will keep your name, NHS number and contact details confidential and will not pass this information to Xenikos. [NHS/other site] will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from Xenikos and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Xenikos will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. Xenikos may forward information about you (again, without any identifying information) to its service providers, for activities related to the study, such as laboratory analysis.

[NHS/ other site] will keep identifiable information about you from this study [for x years after the study has finished/ until x].

Xenikos will collect information about you for this research study from your medical records. Identifying information about you that is included in your medical records will not be shared with Xenikos. We will use this information for the purpose of the research study.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, including future research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

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. The trial may also be registered on national registries and a summary of the results may be posted on publicly accessible databases (such as https://www.clinicaltrialsregister.eu or other national databases), if required by local laws or regulations.

<All other countries specific language, please delete for UK>

Your privacy is very important to us. The study doctors will do everything they can to protect it. The study doctors can protect your records if there is a court case. However, some of your medical information may be shared if required by law. If this happens, the study doctors will do their best to make sure that any information that goes out to others will **not** identify you.

Your confidentiality is one of our main concerns. We will do our best to make sure that the personal information in your medical record is kept confidential (private). However, we cannot promise total privacy.

To make sure the study is running ethically, some government agencies or other groups may need to access part of your medical records. For this study, those groups include:

- [Institution]
- The Center for International Blood and Marrow Transplant Research (CIBMTR)
- The National Marrow Donor Program (NMDP)
- The National Institutes of Health (NIH), which include the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI)
- Data and Coordinating Center of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
- Data Safety and Monitoring Board (DSMB), not part of [Institution]
- [Study investigators/ Study doctor(s) at this institution]
- Food and Drug Administration (FDA)
- Regulatory authorities, both local and from other countries
- Xenikos, BV (Xenikos) (the study sponsor)
- Other authorized study organizations that represent Xenikos
- Study monitors

Information from this study will be put in a public data repository when the study is over, but your name and other personal information will not be included. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Study information may also be used for research in the future. These projects could be related to your disease or similar diseases, or development of the study drug.

We might use information from this study to get approval from the government, like the Food and Drug Administration (FDA).

Blood taken during the study may be used for future research. If the study team does this, the blood or tissue will not be attached to you or your name in any way.

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 website will include a summary of the results. You can search this website at any time.

<*US country specific language, please delete for other countries*>

You will **not** be able to access your study results before the study is done. This helps keep the study results accurate and trustworthy.

When the study is complete, you can ask your study doctor for your health information from the study. **By signing this Consent Form, you agree to ask for your results only after the study is done.** You will still have access to your regular medical records.

Data that was collected through the Center for International Blood and Marrow Transplant Research (CIBMTR) about your clinical situation, including follow-up after 180 days, may be shared with the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) and the study sponsors. The CIBMTR collects information on all transplants done in the U.S.

Most research samples will be sent to a repository for processing and storage. A repository is a place that protects, stores, and sends out samples for approved research studies. All research samples will have unique codes that do not identify you, however, a link to this code does exist. The link is stored at the BMT CTN Data and Coordinating Center (DCC). The staff at the repository where your sample is being stored do not have a link to this code. Your research samples will continue to be stored at the repository until they are used for this study to help us understand the two treatments for aGVHD.

8. Stopping Treatment or Leaving the Study

You can choose to stop treatment or to leave the study at any time.

You may also be told to stop the study treatment if:

- It has been 2 weeks since your first dose of T-Guard and you haven't completed all 4 doses
- You don't meet the study requirements

- You need a medical treatment not allowed in this study
- The study doctor decides that it would be harmful for you to continue
- You're having serious side effects
- You have a severe infection
- You become pregnant
- The disease you needed a transplant for comes back
- You cannot keep appointments or take study drugs as directed
- The study is stopped for any reason

If you join this study and decide to stop your treatment early or are asked to leave by your doctor for medical reasons, we will ask you to still visit the clinic for your safety. We'll also ask whether we can still collect information about how you are doing. Even if you leave the study, the information already collected from you will be included in the study evaluation. If you don't want your information to be used, you **must** let your study doctor know.

9. Cost and Reimbursement

You will **not** be paid for joining this study. You will not be paid or reimbursed for any extra expenses (such as travel or meals) from your participation in this study.

A new drug or product may be developed from this study. Xenikos (the study sponsor) will **not** pay you if a commercial product is developed from blood or tissue taken from you during this study.

The cost of the T-Guard is covered by this study. The cost of ruxolitinib is covered through Day 56 by this study. Your doctor will talk with you about taking ruxolitinib after Day 56.

Most of the visits for this study are standard medical care for patients with SR-aGVHD and will be billed to your health insurance company. You and/or your health insurance company will need to pay for some or all of the costs of standard medical treatment in this study.

Some health insurance plans will not pay for costs of care when you take part in a research study. Check with your health plan or insurance company to find out what they will pay.

You or your health insurance company will not be charged for the extra tests or research costs for this study. The extra tests are done to see how the drug works in your body and how your body responds to the drug.

For questions about your costs, financial responsibilities, and/or health insurance coverage for this study, please contact [Center/ Financial Counselor at /Number].

<Additional information for US; please add country specific language or delete>

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

Physical Injury as a Result of Participation

Tell your study doctor or staff if you think you've been hurt because of being in this study. You must contact [contact in case of research-related injury name, address and telephone number].

You'll get medical treatment if you're hurt as a result of this study. You and/or your health insurance company will be charged for this treatment, and you/your health insurance company will be responsible for payment of these charges.

Xenikos will reimburse either you/your health insurance for emergency medical costs (including hospitalization) in the diagnosis and treatment of an injury that is a direct result of this study. This study will **not** pay for medical treatment as a result of unintended injury that is not a direct result of this study.

In case of injury resulting from this study, you don't lose any of your legal rights to seek payment by signing this form.

<Europe country specific language; please delete for other countries>

The Sponsor has affected insurance coverage in accordance to national legislative requirements of the country in which the clinical trial is performed. Such insurance coverage makes provisions for possible compensation to you in the event of injury to your health, which in the light of medical knowledge can reasonably be attributed to your participation in this clinical trial. Covered is all proven damage (being the financial consequences of the injury to health), with the provision that under certain national legislation, the liability of the Sponsor or the party conducting the clinical trial must be proven.

The insurance coverage applies, provided that:

1. The injury or damage does not consist of temporary impairment of health, which is certain or expected;
2. The injury or damage occurs and is reported within the fixed time limit (as per national legislative requirement) either during or after the termination of the clinical trial;
3. You are to immediately report any injury to the clinical trial investigator;
4. You observed the following regulations in case of injury or damage:
    - You are to put yourself under doctor's orders immediately and do everything in your power to further your recovery;
    - You are to inform the Sponsor at once of the situation by means of the clinical trial investigator or by means of contacting the insurer, of which the details are: [insert name of insurer, address, and phone number];
    - If requested, and at the expense of insurer, you will be prepared to undergo a medical examination performed by a doctor of the insurer's choice at the venue where the doctor desires such an examination to be held as well as to supply the doctor with all information so desired by him/her;
    - If requested, at the expense of the insurer, you will have yourself admitted for examination at a hospital or other medical institution designated by the insurer;
    - You will authorize the insurer to see information from third parties;
    - You will provide or have provided to the insurer or its experts any information deemed necessary by the insurer and not withhold any information needed for a determination of the degree of damage, injury, or impairment.

A copy of the insurance certificate may be obtained from the clinical trial investigator.

During the period of the clinical trial, you are authorized to seek other medical treatment only after consultation with the clinical trial investigator.

Notwithstanding the regulations, nothing contained in this ICF shall serve to alter the provisions of the insurance policy as taken out by the Sponsor.

<*US country specific language, please delete for other countries*>

10. Additional Study: Blood Samples for Future Research (Optional)

Please note: This section of the Consent Form is about an additional study that will be done with people who are taking part in the main study. You may take part in this additional study if you want to. You can still be a part of the main study even if you say 'no' to this additional study.

We ask for your permission to store any extra blood samples that are leftover from the main study. These samples will be used for future research.

Your samples will be used only for research and will not be sold. The research done with your samples may help to develop new products in the future. You will not get paid for any samples or for any products that may be developed from current or future research.

If you agree to allow us to store your extra blood samples, here's what will happen:

- These samples may be stored indefinitely for future research.
- Your research samples will continue to be stored at the repository until they are used up for approved research.
- Only research approved by an ethics board will be allowed to use your samples

Changing your Mind

If you agree to allow your leftover blood samples to be used for research, you can change your mind at any time. If you change your mind, please contact [the Principal Investigator at your transplant center] in writing to state that you are withdrawing permission for your leftover blood samples to be used for research. Their mailing address is on the first page of this Consent Form. Any unused samples will be destroyed if you withdraw your permission. If you choose not to participate in this additional research, there will be no change in your care.

Benefits

You will not benefit directly from providing blood samples for this study. Information gained from research on your blood may help doctors learn about, prevent, or treat GVHD, cancer, or other health problems.

Confidentiality and Your Medical Information

The results of GVHD research using your blood will not be part of your medical record and will not be shared with you. If you agree to allow your blood samples to be used for research, your name will not be on the tubes. Only the study doctors or staff working with them will study the results from your blood samples.

Research companies could make a profit (money) from what they learn using the blood samples.

Making Your Choice

Please read each sentence in the Statement of Consent and think about your choice to allow us to store your extra blood samples. After reading each sentence, make your selection by checking one of the boxes. If you have any questions, please talk to your doctor or nurse.

You may also contact our research review board at [IRB's phone number].

No matter what you decide to do, it will not affect your care.

Statement of Consent for Blood Samples for Future Research (Optional)

The purpose of storing blood samples, the procedures involved, and the risks and benefits have been explained to me. I have asked all the questions I have at this time and I have been told whom to contact if I have more questions. I have been told that I will be given a signed copy of this consent form to keep. I understand that I do not have to allow the use of my blood and for research. If I decide to not let you store research samples now or in the future, it will not affect my medical care in any way.

I understand that I can still be a part of the main study even if I say 'no' to this additional study.

I voluntarily agree that leftover blood samples and related information can be stored indefinitely by the BMT CTN Repository for research to learn about, prevent, or treat GVHD, cancer, or other health problems.

❑ I agree to allow my leftover blood samples to be used for future research.

❑ I do <u>not</u> agree to allow my leftover blood samples to be used for future research.

Printed Participant Name	Date (MM/DD/YYYY)
Participant Signature (or Legally Authorized Representative)	Date (MM/DD/YYYY)
Printed Legally Authorized Representative Name (if applicable)	Date (MM/DD/YYYY)

<*US country specific language, please delete for other countries*>

11. Health Insurance Portability and Accountability Act 1 (HIPAA) Authorization to use health information for research

Your local study site will give you a separate form with information about the Health Insurance Portability and Accountability Act 1 (HIPAA). You will need to sign this form as well before you are able to join this study.

12. Informed Consent Form

TITLE: BMT CTN 2002: A Phase 3, Randomized, Open-Label, Multicenter Study, to Compare T-Guard to Ruxolitinib for the Treatment of Patients with Grade III or IV Steroid-Refractory Acute Graft-Versus-Host Disease (SR-aGVHD)

- I have read and understood this Consent Form. The purpose and description of the research study has been explained to me.
- I have had the chance to ask questions and understand the answers I have been given. I understand that I may ask questions at any time during the study.
- I freely agree to be a participant in the study.
- I have had the chance to discuss my participation in this research study with a family member or friend if I choose.
- I understand that…
    - I may not directly benefit from taking part in the study.
    - My name and personal information will not be identified even if information gained during the study is published.
    - I can leave this study at any time and doing so will not affect my current care or prevent me from receiving future treatment.
    - I will be given a copy of this signed consent form.
    - I do not give up any legal rights by signing this form.

_____ _____

Printed Participant Name Date (MM/DD/YYYY)

_____ _____

Participant (or Legally Authorized Representative) Signature Date (MM/DD/YYYY)

_____ _____

Printed Legally Authorized Representative Name (if applicable) Date (MM/DD/YYYY)

Physician certification

I certify that I have provided a verbal explanation of the details of the research study, including the procedures and risks. I believe the participant has understood the information provided.

Printed Counseling Physician Name	Date (MM/DD/YYYY)
Counseling Physician Signature	Date (MM/DD/YYYY)

Interpreter certification (if needed)

I certify that I have provided an accurate interpretation of this consent form. I believe the participant has understood the information provided.

Printed Interpreter Name	Date (MM/DD/YYYY)
Interpreter Signature	Date (MM/DD/YYYY)