Informed Consent to Participate in Research

BMT CTN 1902

Phase II Multicenter Trial of anti-B Cell Maturation Antigen Chimeric Antigen Receptor T Cell Therapy for Multiple Myeloma Patients with Sub-Optimal Response After Autologous Hematopoietic Cell Transplantation and Maintenance Lenalidomide

Your Name: _____

Principal Investigator:

Insert local PI information

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

The ethics of this study have been reviewed and approved by the National Marrow Donor Program Institutional Review Board.

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're being asked to join because:

- You're ≥ 18
- You have multiple myeloma
- You have already received some treatment for it and had an **autologous transplant** (uses your own cells) within the last year
- You have received **maintenance therapy** with lenalidomide for at least 3 months after your transplant
- Your multiple myeloma has not responded to treatment as well as your doctors would have liked

The usual treatment for people with multiple myeloma is an autologous transplant, followed by maintenance therapy. **Maintenance therapy** commonly uses a drug by the name of lenalidomide and has the objective to delay the time your myeloma returns.

We're doing this study to see if CAR T-cell therapy can treat multiple myeloma when standard therapy didn't work. **CAR T-cell therapy** uses your own cells that have been treated in a lab so they can attack cancer cells.

If you join, you'll be in the study for about 15 months and get:

- **CAR T-cell therapy**. This takes about 3 months. It includes having your blood cells collected, getting chemotherapy (chemo), getting CAR T-cells, and recovery.
- **Maintenance therapy**. This will last about 12 months. You will take a pill called lenalidomide almost every day.

Your blood cells and bone marrow will also be collected and may be used for future research. Researchers will use it to study how the body processes the drugs and recovers from treatment.

Some possible risks and benefits of joining the study include:

> **Possible Risks:** The treatment may not work, and you may have serious side effects.
> **Possible Benefits:** The treatment may keep the multiple myeloma from coming back for some time. Also, doctors may learn how to treat it better in future patients.

If you do **not** join the study, you have other treatment options, such as:

- Other medicines, radiation, or a combination of medicines and radiation
- Joining another clinical trial. Talk with your doctor to see if there is a trial you can join.
- Treatment for your symptoms, but no treatment for multiple myeloma at this time

Key points:

- Being in any 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 quit at any time. If you decide to quit 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 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. No one can force you to join this study.

2. Study Purpose

We are doing this study to see if CAR T-cell therapy and maintenance therapy with the drug lenalidomide can help delay multiple myeloma from coming back.

CAR T-cell therapy is a treatment made of your own immune cells (or T cells). CARs, or chimeric antigen receptors, are added to your T cells in a lab. Doctors think that these receptors will help your T-cells find and attack the myeloma cells.

The specific CAR T-cell therapy in this study, bb2121, has **not** been approved by the U.S. Food and Drug Administration (FDA) to treat multiple myeloma that has already been treated. This study is registered with the FDA, and they will monitor it for safety.

3. Study Treatment and Tests

You will receive CAR T-cell therapy (also called bb2121).

Before Your Treatment

You'll need to have several tests to see if you can be in the study. These tests are part of your regular care. They would be done even if you decide not to join this study. The tests include:

- Medical history and physical exam
- Blood tests to check:
  - The number of different blood cells you have (cell counts)
  - For infections, including HIV (human immunodeficiency virus)
  - How well your blood clots
  - How well your liver and kidneys work

- Tests to see how well your heart is working
- Test to measure oxygen levels in your blood (pulse oximeter)
- Tests to measure the multiple myeloma
- A pregnancy test (if you could be pregnant)

These tests to check if you are eligible for the study are shown in **Table 1**.

During the Study

If you join the study, here's what will happen:

1. Apheresis for CAR T-cell Therapy

Approximately 14 days after you join the study, we will take some immune cells (T cells) from your blood during a procedure called leukapheresis. Your T cells will be used to make the bb2121 T cells. You will be asked to visit your study doctor or other blood collection location your study doctor tells you to go to for the collection of some of your immune cells (leukapheresis). During this procedure, you will be connected to a machine for 2 to 4 hours. You will have an intravenous (IV; into a vein) line placed in each arm. Sometimes the veins in the arm do not allow enough access to the blood, in which case a central intravenous access (catheter/central line) may need to be placed, usually at one side of your neck. Placing a catheter/central line provides an easy way to collect your cells without repeated IV access. Blood is taken out of one of the IVs and is sent through a machine that collects the immune cells, and the rest of the blood is then given back to you through the second IV access. You will be monitored carefully during the procedure. An additional blood sample will be taken to look for infections that might be accidentally passed to someone in contact with your blood cells (hepatitis, HIV etc.), like if you were donating blood.

The immune cells that are collected will be sent to a laboratory. Some of your cells may be stored for future research. The rest will be used to make your CAR T-cell therapy. Your T cells will be separated from the rest of the immune cells and then modified to make the bb2121 T cells. A new gene will be inserted into your T cells using a genetically modified virus. The virus is modified to decrease the chance the virus would make you sick, but the virus will help the T cells recognize the multiple myeloma cells in your body. The process to modify your T cells into bb2121 T cells will take approximately 4 to 5 weeks to complete. Once the process is completed, the laboratory will freeze and store the bb2121 T cells. The frozen bb2121 T cells manufactured for you will be shipped to the study site when you are ready for the treatment and infused back into your blood.

This is not standard care, and the study will pay for it. If you have an unsuccessful initial apheresis, you may proceed to a second apheresis in order to make your CAR T-cell therapy, although success of manufacturing bb2121 cannot be guaranteed by Celgene/BMS

2. Chemotherapy

About 1 month after your cells are turned into bb2121, you will start the chemotherapy to prepare your body to receive the CAR T cells. This chemotherapy helps make room for the CAR T cells. You'll receive 2 chemotherapy drugs: **fludarabine** and **cyclophosphamide.** They are given to you through an intravenous (IV) infusion on 3 different days.

This is not standard care, and the study will pay for the chemotherapy drugs.

Doctors will check your health before you get the chemotherapy. If you are not healthy enough to receive it, you may not be able to receive the CAR T-cell therapy. Your doctor will talk to you about other treatment options if this happens.

Table 1: Tests before CAR T cells

Study Tests	Before you join the study	Before you get chemo	Before you get CAR T-cells
Healthy history, physical exam, height, and weight	X	X	X
Heart tests	X		
Blood test to see how well your blood clots		X	
Blood tests for cell counts, and to see how well your liver and kidneys work	X	X	X
Pregnancy test (if you're able to have children)	X	X	
Test to see how much oxygen is in your blood	X		
Blood and urine tests to measure myeloma cells	X	X	
Bone marrow test to measure myeloma cells		X	
Tests for side effects and infections	X	X	X

3. CAR T-cell therapy

Within 3-17 days after chemotherapy, you will receive the CAR T cells through an IV infusion. This is not standard care, and the study will pay for the CAR T cells.

Doctors will check your health before you get the CAR T cells. If you are not healthy enough to receive them, your doctor may wait and check again later. If you still aren't healthy enough after 2 weeks, you may have to get the chemotherapy again, or you may not be able to get the CAR T-cell therapy. Your doctor will talk to you about other treatment options if this happens.

Doctors and nurses will watch you closely after your CAR T-cell therapy. You will see the doctor and have tests to see how it's working and if you have any side effects. The schedule of tests is in **Table 2**. Most of these are standard care and your health insurance will be billed.

Table 2. Tests after CAR T-cell therapy

Test	Before you start maintenance	Days after you get CAR T cells										
		4	7	10	14	21	30	60	90	180	270	365
Health history, physical exam, weight and height	X	X	X	X	X	X	X	X	X	X	X	X
Blood tests for cell counts, and to see how well your liver and kidneys work	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (if you're able to have children)	X						X	X	X	X	X	X
Blood tests to see how your immune system is working							X	X	X	X	X	X
Blood, bone marrow and urine tests to look for multiple myeloma cells							X	X[1]	X	X	X[2]	X
Tests for side effects and infections	X	X	X	X	X	X	X	X	X	X	X	X

[1] No bone marrow performed at day 60

[2] Bone marrow performed only if determined by the doctor to be needed based on blood test results

4. Maintenance Therapy

About 1-6 months after the CAR T-cell infusion, you will start taking the pill **lenalidomide**. Before you start lenalidomide, your doctor will review your health to confirm you have recovered from receiving your CAR T-cells. You'll take it each day for 21 days, then you'll have 7 days off. You'll repeat this schedule (called a cycle) for about 12 months. You will receive 1 cycle of lenalidomide at a time. Your doctor will talk with you about ordering, receiving, and taking lenalidomide. If the multiple myeloma comes back, you'll stop taking it. Lenalidomide will be given to you for free while you are on this study.

We will watch your health closely while you're taking lenalidomide. We may change your dose based on how your body handles the treatment.

You will need to visit your clinic for several checkups and tests during maintenance therapy. These checkups will happen at the same time as the checkups required after your CAR T-Cell therapy. These tests are shown in **Table 2.** They are standard for people taking lenalidomide maintenance therapy.

The study will take about 15 months and will include 40 participants.

Stopping Treatment

We'll stop the treatment if:

- The multiple myeloma comes back or gets worse
- You have serious side effects

- You're pregnant
- You don't follow the study directions
- You decide to leave the study
- Your doctor thinks it's not safe for you to be in the study anymore

Sample Collection

Throughout the study, we will collect blood and marrow samples to:

- Check if the treatment is working. This is a standard way to check the multiple myeloma.
- Check your immune response after CAR T-cell therapy. This is not standard care.
- Store them for future research. This is not standard care.

Table 3: Schedule for collecting samples

Sample	During leukapheresis	Before chemo	Days after you get CAR T-cells											If your disease returns
			4	7	10	14	21	30	60	90	180	270	365	
Standard of Care (SOC) Blood		X	X	X	X	X	X	X	X	X	X	X	X	X
Research Blood		X						X		X			X	X
SOC Bone Marrow		X						X		X		X[1]	X	X
Research Bone Marrow		X						X		X			X	X
T cells	X													

[1] Bone marrow performed only if determined by the doctor to be needed based on blood test results

4. Risks and Benefits

Possible Benefits

The study treatments may keep the multiple myeloma away longer. Also, doctors may learn how to treat it better. This could help people with multiple myeloma in the future.

Possible Risks

You may have side effects during the study. Side effects can range from mild to severe. Your health care team may give you medicine to help with certain side effects, like an upset stomach. In some cases, side effects can last a long time or may never go away.

bb2121 – CAR T-cell therapy

Likely (May happen in more than 10% of patients)	**Less Likely** (May happen in 10% or fewer patients, but more than 1%)	**Rare, but Serious** (May happen in 1% or fewer patients)

• Abnormal liver tests
• Anemia (low red blood cells) which may require blood transfusions
• Cytokine Release Syndrome (CRS). This is a very strong response from your immune system. You could have fevers, dizziness, fluid in your lungs, nausea, headache, fast heartbeat, low blood pressure, or low oxygen level in the blood. CRS can be severe or fatal.
• Diarrhea, nausea, or vomiting
• Dizziness
• Fast heartbeat
• Fatigue
• Fever
• Headache
• Low blood pressure
• Low levels of calcium, potassium or sodium in your blood. You could feel very tired, have muscle weakness, cramps or an irregular heartbeat
• Low number of cells that help your blood clot (platelets)
• Low number of white blood cells with or without fever
• Severe damage to your brain and nervous system. This is called neurotoxicity. You could be confused or disoriented, have difficulty speaking, feel extremely sleepy, have seizures, or have swelling or bleeding in your brain Pain affecting your joints
• Shivering or chills
• A problem with the immune system that prevents it from making enough antibodies, called immunoglobins,
	• Difficulty or trouble speaking
	• Dizziness upon standing
	• Excess fluid in the body
	• Low oxygen level in your blood. You could feel short of breath, confused or drowsy
	• High level of proteins in your blood, including:
	  ○ C-reactive protein, which may be a sign of inflammation
	  ○ Ferritin, which may be a sign of iron levels
	  ○ Bilirubin, which may be a sign of how well your liver works
	• Muscle pain
	• Shaking or twitching (tremor)
	• Sleepiness
	• Neurotoxicity, which can be severe
	• Abnormal or altered brain function (encephalopathy)
		• Difficulty or slowed thinking
		• The sudden rapid death of cancer cells, in response to treatment, causing release of their contents into the bloodstream which can interfere with the function of the kidneys, heart, nervous system, and other organs (tumor lysis syndrome).

Likely (May happen in more than 10% of patients)	Less Likely (May happen in 10% or fewer patients, but more than 1%)	Rare, but Serious (May happen in 1% or fewer patients)
that are important for fighting infection • Confusion • Swelling (edema) • Chest infection (upper respiratory tract infection) • Cough • Shortness of breath with or without exercise		

Blood or Organ Donation

You will not be allowed to donate blood, organs, sperm or semen, egg cells or other body fluids for at least 12 months after the last dose of chemotherapy.

There is no information about the risks of tissue donation following treatment with bb2121. The total length of time to refrain from donation of blood, organ, sperm or semen, egg cells or other body fluids after bb2121 treatment is not known. Therefore, any decision regarding donation of blood, organ, sperm or semen, egg cells or other body fluids after bb2121 infusion should be discussed with the study doctor.

Risk of HIV testing

To make CAR T cells, doctors use a molecule designed to carry the instructions into T cells, called a vector. Viruses are often used as vectors because they know how to get into the right part of the cell to deliver the instructions. The vector used to make bb2121 CAR T cells comes from the human immunodeficiency virus (HIV). The part of the virus that causes infection has been significantly changed to lower the risk of disease. So far, no patients who have received bb2121 CAR T cells or cells using viral vectors have developed HIV from the gene-modified cells.

Some blood tests may say you have HIV after getting this study treatment. This does **not** mean that you have HIV infection. If you have an HIV test in the future and it comes back positive, tell the doctor that you have received CAR T cell therapy as part of this study. A subsequent or more sensitive HIV test will be able to establish your viral status. The doctor may still have to follow laws and report the initial positive test result, even if that initial result is false or temporary, to the local health department.

Risks of Vector (Virus) Replication (Copying)

The virus used to make the bb2121 CAR T cells in this study was genetically modified to keep it from duplicating or spreading. However, there is a risk that the virus could get the ability to

multiply. This is called a replication competent lentivirus (RCL). Your doctors will watch you closely for signs of RCL as long as the bb2121 CAR T cells are in your blood. Doctors don't know the risks of RCL, but it could make you sicker than you are now.

Risks associated with antibody formation

You could develop a strong immune response against the CAR T cells. Your immune system could kill them. Doctors don't think this is harmful. However, if you have fewer CAR T cells, it is less likely they will kill the multiple myeloma.

Your immune system may also develop antibodies (proteins) that cause an allergic reaction, like rashes, itching and fever. More serious allergic reactions can cause shortness of breath and low blood pressure. If this happens, you may need to be in the hospital for treatment.

Risk of Cytokine Release Syndrome (CRS) and Neurotoxicity

Cytokine release syndrome is a very strong response from your immune system. You could have fevers, dizziness, fluid in your lungs, nausea, headache, fast heartbeat, low blood pressure, or low oxygen level in the blood. CRS can be severe or fatal. Neurologic symptoms may include altered mental status, aphasia (unable to speak or write and unable to understand spoken or written words), altered level of consciousness, and seizures or seizure like activity, and can accompany CRS or occur alone.

Uncontrolled growth of bb2121 CAR T cells

bb2121 CAR T-cells will multiply after being put in your body. This is how they work to treat the multiple myeloma. The bb2121 CAR T cells could grow too much and out of control. In this event, your study doctor may wish to inactivate the bb2121 T cells. This can be done by giving drugs called corticosteroids. If the uncontrolled bb2121 T cell growth cannot be controlled by corticosteroid treatment, your study doctor may recommend chemotherapy, like what is usually administered for your cancer. The main risk of short-term corticosteroids or the use of chemotherapy is an increased risk of infections. No uncontrolled growth of bb2121 T cells has been seen to date.

Cyclophosphamide – Chemotherapy drug you take before CAR T-cell therapy

Likely (May happen in more than 20% of patients)	**Less Likely** (May happen in 20% or fewer patients, but more than 2%)	**Rare, but Serious** (May happen in 2% or fewer patients)
• Blood in urine • Digestive problems, such as nausea, vomiting, diarrhea, loss of appetite, pain in belly • Feeling tired • Hair loss • Infection, especially when white blood cell count is low	• Allergic reaction. This may cause rash, low blood pressure, difficulty breathing, and swollen face or throat • Low red blood cell count (anemia). You may need blood transfusions • Loss of sperm. You may not be able to have children.	• A new cancer, such as leukemia (a blood cancer) • Brain swelling. You may have dizziness and confusion. • Heart damage or heart failure. You may have shortness of breath, swelling, cough or tiredness

• Mouth sores • No periods (menstrual cycles). You may not be able to become pregnant. • Skin and nail changes, including rash	• Low platelet count. You may bruise or bleed easily.	• Scarred lungs. You may have shortness of breath or fluid around your lungs.

Fludarabine – Chemotherapy drug you take before CAR T-cell therapy

Likely (May happen in more than 20% of patients)	**Less Likely** (May happen in 20% or fewer patients, but more than 2%)	**Rare, but Serious** (May happen in 2% or fewer patients)
• Low red blood cell count (anemia). You may need blood transfusions • Cough • Feeling tired or irritable • Infection, especially when white blood cell count is low • Low platelet counts. You may bruise or bleed easily. • Pain	• Chills • Confusion • Damage to your brain, lungs, or other body parts. You may feel tired, short of breath, or have difficulty thinking • Feel "pins and needles" in your arms and legs • Mouth sores • Nausea, vomiting, loss of appetite	• Blood in urine • Changes to your vision • Kidney damage. You many require dialysis. • Liver problems • Seizures

Lenalidomide – Pill you take after CAR T-cell therapy

Likely (May happen in more than 10% of patients)	**Less Likely** (May happen in 10% or fewer patients, but more than 1%)	**Uncommon to Rare, but Serious** (May happen in 1% or fewer patients)
• Abnormal liver lab tests • Allergic reaction • Altered sense of taste • Blood clots • Change in your sense of taste and touch • Constipation • Cough • Diarrhea • Dizziness	• Abnormal heart beats • Blood not getting to arms or legs • Breathing problems • Bruise • Cancer • Damage to your kidneys due to rapidly dying cancer cells. Your kidneys could also stop working. • Destruction of red blood cells (hemolysis)	• Severe allergic reaction. You may have skin peeling, fever, swollen glands with inflammation of the liver, kidneys, lungs, or heart. • Swollen lungs • Thyroid problems • Very fast destruction of cancer cells. This is called tumor lysis syndrome. It can cause changes in your blood and kidney damage. It can be severe or fatal.

Likely (May happen in more than 10% of patients)	**Less Likely** (May happen in 10% or fewer patients, but more than 1%)	**Uncommon to Rare, but Serious** (May happen in 1% or fewer patients)
• Dry skin • Feeling sad • Feeling short of breath • Feeling weak, tired and unwell • Fever and chills • Headache • Indigestion • Itching • Kidney failure • Low appetite • Low number of white blood cells with or without fever. • Low number of red blood cells (anemia) • Low number of cells that help your blood clot (platelets) • Nosebleed • Not sleeping well • Pain, affecting your muscles, joints and chest • Pneumonia or other infections • Nausea or vomiting • Shaking • Stomach Pain • Swelling • Sore throat • Stuffy nose • Vision changes • Weight loss	• Slower movement of food through your intestines • Diabetes • Dry mouth • Excessive sweating • Fainting • Fall • Feeling drowsy and listless • Feeling moody • Fluid loss • Heart attack • Heart stops working • High or low blood pressure • Abnormal levels of iron, phosphorus, magnesium, sodium and calcium in your blood • Infection caused by a virus • Liver damage and abnormal liver tests • Muscle weakness • Night sweats • Skin redness • Stroke • Sudden increase in tumor size • Swollen skin or blood vessels • Tingling skin • Too much uric acid in your blood	

Risk to Unborn Babies

Because of the risks related to the study treatments, you must take precautions (such as contraception) that you (if you are a female subject) or your female partner (if you are a male subject) do not become pregnant during the study.

The risks to an unborn child (fetus) or nursing child from bb2121 are not known at this time. bb2121 should not be administered to pregnant or nursing women.

Lenalidomide can cause severe birth defects or death of a baby if the mother or the father is taking this medicine at the time of conception or during pregnancy. **Do not get pregnant while you're taking lenalidomide.**

If you are a woman:

If you're pregnant or nursing, you **cannot** be in this study. You must not be pregnant and must not become pregnant during the study and for at least 12 months after treatment with cyclophosphamide and/or fludarabine chemotherapy and for 28 days after completion of the lenalidomide.

There is no data to provide any recommendation concerning the total length of time to prevent pregnancy after bb2121 treatment. Therefore, any decision regarding avoidance of pregnancy and contraception after bb2121 infusion should be discussed with the treating physician.

If you are able to become pregnant, the study doctor will discuss with you the options for, as well as the correct and consistent use of effective methods, to successfully prevent pregnancy during this study. Your chosen form of contraception must be effective by the time you start apheresis. Anyone who can become pregnant must avoid any sexual activity that can lead to pregnancy or, if you engage in sexual activity that could lead to pregnancy, you must use **at least 2 forms of effective birth control** while in this study and for 28 days after, to include 12 months after treatment with chemotherapy. Effective birth control includes:

- Birth control pills
- Injectable birth control (Depo-Provera, Norplant)
- An IUD (intrauterine device)
- Condoms
- Spermicide
- Cervical cap or a diaphragm

You do not need to use birth control if you or your partner:

- Had your ovaries and uterus removed, **or**
- Had your ovaries removed, **or**
- Went through menopause

Tell your doctor right away if you become pregnant during the study. Your doctor will talk with you about the risks to your child and your options.

If you suspect that you have become pregnant during the study, within 12 months after chemotherapy, any time after the bb2121 T cell infusion, or within 28 days of completion of lenalidomide you must tell your study doctor right away. During your study visits, the study doctor may ask you for more information about any pregnancy until its completion and afterwards until up to 1 year of the newborn baby, to see if there are any effects of the study treatments.

It is unknown if bb2121 is excreted in human milk and can be transferred to a breast-feeding child. Females must agree not to breast-feed during the study. The total length of time to avoid breastfeeding after bb2121 treatment is not known. Therefore, any decision regarding breastfeeding after bb2121 infusion should be discussed with the treating physician.

If you are a man (including those who have had a vasectomy):

If you are a male, by signing this consent form, you agree to avoid getting your female partner pregnant during the study, within 12 months after chemotherapy, any time after the bb2121 T cell infusion, or within 28 days of completion of lenalidomide. If you engage in sexual activity, the study doctor will discuss with you the options for, as well as the correct and consistent use of effective methods, to successfully prevent pregnancy during this study. You and/or your partner's chosen form of contraception must be effective by the time you start apheresis. Anyone who can become pregnant must avoid any sexual activity that can lead to pregnancy or, if you engage in sexual activity that could lead to pregnancy, you must use **at least 2 forms of effective birth control** while in this study and for 28 days after, to include 12 months after treatment with chemotherapy. Effective birth control includes:

- Birth control pills
- Injectable birth control (Depo-Provera, Norplant)
- An IUD (intrauterine device)
- Condoms
- Spermicide
- Cervical cap or a diaphragm

You do not need to use birth control if your partner(s):

- Had their ovaries and uterus removed, **or**
- Had their ovaries removed, **or**
- Went through menopause

The total length of time to prevent pregnancy after bb2121 treatment is not known. Therefore, any decision regarding pregnancy and contraception after bb2121 infusion should be discussed with the study doctor.

You must tell your study doctor right away if during the study, for at least 12 months after lymphodepleting chemotherapy, at any time after bb2121 infusion or within 28 days of

completion of lenalidomide if you learn that your female partner is pregnant. The study doctor will ask if the results of medical checks during and after your partner's pregnancy can be shared with him/her and the study sponsor, to increase understanding of the medicine's safety. She will be asked to sign a separate consent to provide this information. Your partner does not have to provide information about her pregnancy unless she wants to do so.

If you have any questions about this information, please ask your study doctor**.**

Pregnancy and Lenalidomide REMS®

You have been informed of the risk of birth defects. If you are female, you agree not to become pregnant while taking lenalidomide. For this reason, lenalidomide is provided to patients under a special distribution program called Lenalidomide REMS ®. In order to participate in this study, you must register into and follow the requirements of the Lenalidomide REMS® program of Celgene Corporation. This program provides education and counseling on the risks of fetal exposure, blood clots and reduced blood counts. You will be required to receive counseling every 28 days during treatment with lenalidomide, follow the pregnancy testing and birth control requirements of the program that are appropriate for you and take telephone surveys regarding your compliance with the program.

You understand and agree to receive counseling and to comply with the pregnancy precaution requirements of the Lenalidomide REMS® program. You will be registered in the Lenalidomide REMS® program.

Other risks of being in this study:

Because bb2121 is made from your blood cells in a process that takes several weeks, there is a chance that you could become too sick while you are awaiting infusion, and not be able to receive bb2121.

- **Risks of Apheresis (cells collected from your blood)**

The risks of apheresis include:

- A hole could be poked in your lung
- Blood flow could be blocked in your vessels or heart by an air bubble
- Bleeding
- Infection
- Low blood cell counts
- High or low blood pressure

After the apheresis procedure, you may experience temporary discomfort, including irritation, swelling, pain or bruising at the place where the needles were inserted into your veins to collect and return the blood. Apheresis can also occasionally cause nausea, vomiting, fainting, seizures, blood loss, infection, skin rash, flushing, hives, numbness and tingling, or swelling of your feet or

ankles. Pain can usually be managed with pain medication.

- **Drug Interactions**

Some drugs react with each other, so tell the study doctor or nurse about any other drugs, treatments, or medicines you're taking. This includes non-prescription or over-the-counter medicines, vitamins, and herbs. Also, tell them about any changes to your medicines while you're in the study.

- **Treatment may not work**

The multiple myeloma may come back, even if it went away for a short time.

- **New blood cancer or non-hematologic malignancy**

We don't know if lenalidomide or other drugs could cause new blood cancers or other non-hematologic malignancies. Researchers are still studying this. Your doctor will watch you closely for signs of a new blood cancer or non-hematologic malignancy. You are also encouraged to resume usual, age-appropriate cancer screening. We will give you any new information that we learn about this.

- **Serious infections**

It may take many months for your immune system to recover from the chemotherapy and lenalidomide. You have a higher risk of infection during this time. We will give you medicine to lower your risk of infection, but they may not work. If you have an infection, you may have to stay in the hospital longer or return to the hospital. Many people get better, but some infections can cause death.

There is a small chance that when your CAR T cells are being made in the lab, they could be exposed to bacteria, and that you could get an infection from the infusion. The cells will be tested for different infections before they are given to you.

Unforeseen Risks

Other new risks might appear at any time during the study. These risks might be different from what is listed in this form. There may be some unknown or unanticipated side effects from this treatment. The study team will do everything they can to keep you safe and lower your risk of side effects.

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 at any time you are considering leaving the study, talk to your study doctor about your health and safety.

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 for Principal Investigator or study team]

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]

You must tell [insert name of Principal Investigator] if you decide to leave the study.

You could have serious health risks if you stop treatment during the chemotherapy before you receive your CAR T-cell therapy. 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.

Your other choices may include:

- A blood or marrow transplant (BMT) using your own cells (autologous) or cells from a donor (donor)
- Treatment with other drugs and/or radiation
- Joining another clinical trial, if available (check with your doctor)
- Treatment for your symptoms, but no treatment for multiple myeloma at this time

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 CAR T-cell therapy and lenalidomide or the risks and benefits of taking part in the study. Your 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 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

Your privacy is very important to us. The study doctors, study sponsor, and other groups with access to your study-related medical information 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:

1. /Institution/
2. The Center for International Blood and Marrow Transplant Research (CIBMTR)
3. The National Marrow Donor Program (NMDP)
4. The Food and Drug Administration (FDA)
5. Office of Human Research Protection (OHRP)
6. The National Institutes of Health (NIH), which include the National Heart, Lung, and Blood Institute (NHLBI) and the National Cancer Institute (NCI)
7. Data and Coordinating Center of the Blood and Marrow Transplant Clinical Trials Network (BMT CTN)
8. Data and Safety Monitoring Board (DSMB), not part of /Institution/
9. Study investigators.
10. Celgene, the company that makes lenalidomide and bb2121 CAR T-cell therapy

Study information may be:

- Published or presented at scientific meetings. Your name and other personal information will not be used.
- Used for future research. These projects could be related to your disease or similar diseases, or development of the study drug.
- Used to get approval from the government, like the Food and Drug Administration (FDA).

For purposes of chain of identity to track your T cells from the time of collection through the processing and manufacturing of bb2121T cells, and ultimately to ensure that your modified T cells are returned to the study staff for administration to you, the following identifying information will be collected:

- Your full name and initials
- Your date of birth

Your full name and date of birth will be communicated to the Celgene scheduling and manufacturing staff. This information will also be listed on the cell collection bag during the leukapheresis process, and then transferred to other containers throughout the making of bb2121T cells. Ultimately, this information will be confirmed by the study staff and the nurses in the administration unit prior to administering bb2121 T cells to you. Your name and date of birth

will be maintained in a separate limited access database and not together with any other clinical information. Only staff who need to use this information will have access to it.

All the other clinical information collected for this study will be processed without your name, ID number or any other information which allows your identification.

A description of this clinical trial will also be available on http://www.ClinicalTrials.gov/, as required by U.S. Law. This website 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.

You will **not** be able to access your individual study results before the study is done as this helps keep the study results accurate and trustworthy, but your doctor will discuss your clinical results with you.

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. You will also be able to see results from the study when it's done.

Data about your health, including follow up after 12 months, may be obtained by the BMT CTN from the CIBMTR, which collects information on all US transplants.

In order to obtain lenalidomide free of charge from Celgene, your name, address, phone, date of birth and the fact that you are participating in this trial will be disclosed to Celgene and its agents or vendors that supply lenalidomide and administer the Lenalidomide REMS® program. By signing this consent form, you agree to this disclosure.

Optional use of your blood cells and bone marrow for future research

- If you agree, your blood cells and bone marrow samples will be used for future research. The samples will not be attached to you or your name in any way. Results of the research done with these samples will **not** be given to you.

- The samples will be sent to the BMT CTN Repository for processing and storage. All research samples will be given a bar code that cannot be linked to you.

- Doctors and researchers may use the stored samples for BMT CTN research. In the future, other researchers can use the unused samples and data. They will need to apply to study the samples. The BMT CTN Steering Committee and/or Executive Committee must approve each request before they will share samples or information with researchers. This is to make sure that the researchers are qualified, and that the research is high quality.

- Genetic information from your stored samples might be used in **genome-wide**

association (GWA) studies for future research done or supported by the National Institutes of Health (NIH). GWA studies help scientists find genes involved in disease or treatment. Each study can look at thousands of genetic changes at one time.

- If your samples are used in a GWA study, the researcher is required to add your test results and information into a shared, public research database. The database is managed by the National Center for Biotechnology Information (NCBI). The NCBI will never have any information that would identify you or link you to your information or research samples.

- A federal law called the **Genetic Information Nondiscrimination Act (GINA)** makes it illegal for health insurance companies, group health plans, and employers of 15 or more persons to discriminate against you based on your genetic information. Health insurance companies and group health plans may not request your genetic information that we get from this research and may not use your genetic information when making decisions about your health insurance. This federal law will **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

8. Leaving the Study

You can choose to leave the study at any time.

You may also be told to leave the study for reasons such as:

- 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 to you to stay in the study.
- You're having serious side effects.
- You become pregnant.
- You cannot keep appointments or take study drugs as directed.
- The study is stopped for any reason.

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 also 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. Celgene or others will not pay you if a commercial product is developed from blood or tissue taken from you during this study.

Most of the visits for this study are standard medical care for people with multiple myeloma 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 if they will pay.

Your chemotherapy, CAR T-cell therapy, and maintenance therapy will be paid for by this study. Lenalidomide will be paid for by the study for 1 year. After that your doctor will discuss what treatment is best for you.

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

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'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. The study sponsor and The National Institutes of Health will not pay for medical treatment as a result of unintended injury. The study contributor, Celgene Corporation will reimburse for reasonable and necessary medical expenses incurred by study subjects for emergency medical care including hospitalization, diagnosis and treatment of study subjects' injury arising directly from the study drug, provided that the study drug was used in accordance with the protocol.

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

10. Long-Term Follow-up

Treatment of CAR T cells are novel, and the US Food and Drug Administration (FDA) recommends that patients who receive these therapies be followed for 15 years to assess whether late side effects may occur. You will be followed for this study for 12 months.

You will be offered a separate informed consent to share your health data related to this treatment with the CIBMTR for research purposes. The information related to complications and response to your treatment during this study and beyond 12 months will be shared with the CIBMTR. There are no additional requirements from you to participate beyond to what will be done as part of your routine medical care. More details about the CIBMTR will be included on that separate informed consent document.

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).

TITLE: BMT CTN 1902: Phase II Multicenter Trial of anti-B Cell Maturation Antigen Chimeric Antigen Receptor T Cell Therapy for Multiple Myeloma Patients with Sub-Optimal Response After Autologous Hematopoietic Cell Transplantation and Maintenance Lenalidomide

- 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 and provide additional laboratory samples.
- I freely agree to additional testing over that required by standard of care.
- 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.

_____ _____

Participant Name (or Parent/Guardian) Date (MM/DD/YYYY)

_____ _____

Participant Signature (or Parent/Guardian) Date (MM/DD/YYYY)

Statement of Consent for Samples for Future Research (Optional)

The purpose of storing 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 or bone marrow 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 voluntarily agree that blood and/or bone marrow samples may be collected and that my related information can be stored indefinitely by the BMT CTN Repository for future research.

Blood samples:

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

❑ I do not agree to allow my blood to be used for future research.

Bone marrow samples:

❑ I agree to allow my bone marrow to be used for future research.

❑ I do not agree to allow my bone marrow to be used for future research.

Participant Name (or Parent/Guardian)	Date (MM/DD/YYYY)
Participant Signature (or Parent/Guardian)	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.

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.

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