Affix Patient Label Here

MT2018-06
Adult

Title of Research Study: Single-Arm, Open Label, Interventional Phase II Clinical Trial Evaluating MGTA-456 In Patients With High-Risk Malignancy

Investigator Team Contact Information: ***Margaret L. MacMillan, MD***

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

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Supported By: Magenta Therapeutics and the National Institutes of Health.

Key Information About This Research Study

The following is a short summary of the research to help you decide whether or not you would like to participate.

What is research?

There are important differences between a treatment that is part of a research study and a treatment that is considered to be the standard of care here and elsewhere:

- Research is focused on learning how to better help people in the future. To accomplish that goal, the research team develops a treatment plan used for all patients with a certain condition. While prior work suggests that the new treatment could be beneficial for that condition, testing in patients is required to know for sure. Even if it helps the majority of people, you as an individual may or may not be helped by the research treatment.
- Standard of care treatments, on the other hand, have known benefits and risks. In situations where the standard of care treatment is not optimal, research treatments may be considered. In contrast to research treatments which follow one treatment plan for all patients, standard of care treatments are often tailored to each patient.

In the setting of blood and marrow transplantation, research and clinical care are often combined. One purpose of this consent document is to tell you what is standard of care and

what research in terms of treatment and follow-up care.

If your doctor is also the person responsible for this research study, please note that she is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Why am I being asked to take part in this research study?

You have a form of blood cancer that makes you potentially eligible for a transplant using umbilical cord blood.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

Umbilical cord blood transplantation has been used in more than 40,000 patients primarily for blood cancers. However, the blood counts are slower to recover after cord blood transplant as compared to bone marrow or mobilized peripheral blood. Slower blood count recovery can result in longer time in the hospital and greater number of transfusions.

To speed up blood count recovery, the number of blood forming stem cells can be multiplied more than 300 times on average in the laboratory prior to giving it to you. As of February 2019, approximately 50 patients have been treated with expanded cord blood, referred to as "MGTA-456", and the time to blood count recovery has been reduced by more than a week with no additional side effects that we can tell so far. Patients have been followed for a more than 2 years. The purpose of this study is to increase the number of patients treated with MGTA-456 and further study the recovery of the blood counts and immune system, evaluate infection risks, transfusion needs and costs.

This study is considered investigational because MGTA-456 is not approved by the Food and Drug Administration (FDA); however this study is being conducted with the FDA's permission under an "Investigational New Drug" (IND) application.

How long will the research last?

If you decide to participate, you will be in this research study for approximately 2 years and 2 months – up to 2 months before transplant with MGTA-456 for pre-study testing and up to two years after transplant for monitoring blood cell and immune recovery. After 2 years, your standard of care follow-up will continue as for any patient undergoing blood and marrow transplant. However, it is possible that you may be contacted if the FDA requests additional information.

What will I need to do to participate?

The treatment plan consists of 4 parts:

1) Pre-transplant evaluation
2) the preparative chemotherapy and radiation given over approximately 1 week,
3) the infusion of the MGTA-456 (the transplant)
4) follow up visits

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

Is there any way that being in this study could be bad for me?

The majority of the risks observed were related to the standard of care treatment, namely infection, graft-versus-host disease, recurrence of the leukemia. These risks have not been altered as far as we can tell. However, it is possible that you could have a reaction to the infusion of MGTA-456 because of one of the chemicals used in the expansion culture or to preserve it while it is frozen. One patient had low blood pressure several hours after the infusion because of bacteria that had not been previously detected. This complication may be less likely moving forward since there will be 2 or more days to check for bacteria in the MGTA-456 before it is infused rather than one day in the past. There are other risks that are possible but not yet observed. For example, there could be risks to receiving too many blood-forming stem cells or the expanded cells might not work properly. It is also possible that immune recovery could be slower because there are fewer immune cells being infused at the time of

transplant.

More detailed information about the risks of this study, can be found under ***"What are the risks of this study? Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, MGTA-456 has led to faster recovery of the white blood cells and platelets and fewer days in the hospital in most of the patients previously treated, although not all patients. It is hoped the information learned from this study will benefit other patients in the future.

What happens if I do not want to be in this research?

You do not have to participate in this research. Instead of being in this research study, your choices may include:

- a standard of care transplant (chemotherapy with or without total body irradiation) using the same cord blood unit without expansion, or possibly marrow or peripheral blood stem cells from a mismatched related donor or matched unrelated donor
- treatment with other drugs or combination of drugs without transplant
- other investigational treatments at this institution or at other research centers
- no further treatment at this time

Your doctors can provide you with additional information regarding your options.

Detailed Information About This Research Study

The following is more detailed information about this study in addition to the information listed above.

How many people will be studied?

We expect about 40 people will be part of this research study over several years.

What happens if I say "*Yes, I want to be in this research*"?

This research treatment (see treatment calendar at the end of this document) will be reviewed in detail with you and any questions you may have will be answered. If you are interested taking

part in the study, you will be asked to sign this consent form. You will be given a copy of the consent form for your personal files.

Immunizations:
To follow how quickly your immune system recovers after transplant, you will have a vaccination against diphtheria, tetanus, whooping cough, hepatitis B, and polio ("Pediarix") and a vaccination against pneumonia ("Pneumovax") at 2 months, 4 months, and 6 months post-transplant.

In addition to the standard procedures and blood tests routinely performed for all patients undergoing transplant, you will have some additional blood testing as detailed in the table below as well as be transplanted with MGTA-456 administered in three bags through your central intravenous line rather than standard cord blood that is administered in one bag.

Research Blood Tests

Before Transplant	**Week or Month After Transplant (Approximate)**									
Up to 2 months prior	**1 week**	**2 week**	**3 week**	**4 week**	**5 week**	**6 week**	**2 month**	**3 month**	**6 month**	**12 and 24 month**
6 tablespoons	5 table-spoons	5 table-spoons	5 table-spoons	5 table-spoons	5 table-spoons	5 table-spoons	6 table-spoons	6 table-spoons	6 table-spoons	5 table-spoons

*Blood tests are done to evaluate the immune system recovery, response to vaccinations, and certain viral infections and engraftment not routinely performed at certain time points.

None of the research related testing results will affect your care or your participation in this study. Neither you nor your health insurance provider will be charged for the cost of research sample processing, storage and testing.

Research studies on your blood cells will be performed in a research laboratory. After the sample arrives in the Translational Therapy Laboratory in the Masonic Cancer Center, it will be labeled with a unique patient code instead of your name or other identifying information. The blood samples will be labelled with your unique code making it difficult for anyone looking at the sample to know it belongs to you.

There may be some leftover blood cells from the samples collected for research purposes. Additionally, there may be extra cells in the product that cannot be given to you due to safety reasons. These cells would otherwise be discarded. With your permission, we would use these cells for research. You will be asked to indicate your decision about future use of leftover samples and extra cells at the end of this document.

What happens if I say "Yes", but I change my mind later?

You can leave the research study at any time even after the infusion of MGTA-456. While it is not possible to get the expanded stem cells back, research blood testing can be discontinued.

If you decide to take part in this study or leave the study, no one will be upset by your decision and your doctors will still take care of you, providing you with standard of care treatments that are available at this institution.

If you stop being in the research, information already collected about you, however, will not be removed from the study database. You will be asked whether the investigator can continue to collect information about your health, such as your medical records. If you agree, this information will be handled the same as the information obtained for the research study.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. This means that your choice not to be in this study will not negatively affect your right to any present or future medical care.

What are the risks of being in this study? Is there any way being in this study could be bad for me? (Detailed Risks)

You may experience some or many of side effects from the standard of care part of this treatment from the chemotherapy and radiation and cord blood. It is possible that the severity or frequency of side effects could be different after MGTA-456 as compared to standard cord blood. The severity of side effects may be mild, moderate or severe, including death. Also, there is always the risk of a rare or previously unknown side effect occurring. If a side effect occurs from the research treatment, your doctors and transplant team will do everything they can to help you feel better.

Other side effects may be related to the extra blood testing that is part of this research. The blood will be obtained from your central intravenous line so it should not cause pain. However,

extra blood tests might make you anemic and it might increase your need for transfusions beyond what you will typically need early after transplant.

Risks of Vaccinations Given to Test Immune Recovery

Pediarix (diphtheria, tetanus, whooping cough, hepatitis B, and polio)
• injection site reactions (redness, itching, pain, swelling, bruising, burning, or a small amount of blood loss) • fever • joint pain • body aches, • loss of appetite • nausea • vomiting • diarrhea

Pneumovax (pneumonia)
• injection site reactions (redness, itching, pain, swelling, bruising, burning, or a small amount of blood loss) • muscle or joint aches or pain • fever • chills • headache • nausea • vomiting • stiffness of the arm or the leg where the vaccine was injected • weakness • fatigue • skin rash

Risks associated with the Standard of Care Treatments are detailed in Appendix attached to this Consent.

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

What do I need to know about reproductive health and/or sexual activity if I am in this study?

Reproductive Risks:

The treatments used in this trial have clear evidence of harm to an unborn baby.
You should not be or become pregnant or father a baby and/or breastfeed while on this research study.

If you are sexually active, both men and women should use at least two effective means of birth control while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable, but least effective, methods of birth control include male condoms (with or without spermicide) and female condoms.

If you or your partner become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You might be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

If you or your partner [are/is] considered to be postmenopausal, you are not required to use contraception while participating in this research study. Postmenopausal women rarely become pregnant. If you or your partner become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other clinical care options will be discussed with you at that time if necessary.

Duration of Study Treatment:
Treatment and follow-up in this study will take approximately 2 years. Your study doctor may discontinue your participation on this study at any time with or without your consent for a number of reasons, including:

- You have side effects that the study doctor considers unacceptable despite changes in drug dose and/or schedule.
- Your disease returns and you need additional chemotherapy or a second transplant.
- Your blood and marrow does not recover and you need a second transplant
- Continuing on treatment, regardless of reason, is not in your best interest.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

All patients having a transplant will be followed for 2 years from transplant on this study and at least once a year thereafter as standard post-transplant follow-up.

Will it cost me anything to participate in this research study?

Taking part in this research study may lead to added costs to you or your insurer if there are side effects related to the research. However, you or your insurer will not be charged for the expansion culture to make MGTA-456 or the extra blood samples specifically obtained for this research study.

You or your insurance company will be responsible for all costs related to the standard of care including but not limited to the cost of purchasing the cord blood unit from the Cord Blood Bank, the chemotherapy (cyclophosphamide, fludarabine), radiation therapy, supportive care, hospitalizations and clinic visits. You will be responsible for any costs your insurance does not cover, such as deductibles and co-payments; however, the transplant will be "prior authorized" by your insurance prior to the pre-transplant screening. In other words, you and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. You should check with the hospital financial team and/or your insurance carrier to verify what services will be covered by your insurance and what you will be responsible to pay.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the Institutional Review Board (IRB), the committee that provides ethical and regulatory oversight of research, and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Masonic Cancer Center, University of Minnesota and/or their designee.
- Any person who provides services or oversight responsibilities in connection with this study.
- Any member of the University of Minnesota workforce who provides services in connection

with this study.

- Any laboratories, individuals, and organizations that use your health information in connection with this study.
- Any federal, state, or local governmental agency that regulates the study (such as the U.S. Food and Drug Administration (FDA), the U.S. Department of Health & Human Services (DHHS), and the Office for Human Research Protections (OHRP)).
- Center for International Blood and Marrow Transplant Research (CIBMTR) and National Marrow Donor Program (NMDP) for the Observational Research Database – this organization collects information on therapies involving donor cells.
- The designated Protocol Review and Monitoring Committees, Institutional Review Boards (IRB) such as the University of Minnesota IRB, Privacy Boards, Data and Safety Monitoring Council and their related staff that have oversight responsibilities for this study.
- Investigators at Magenta Therapeutics who will receive MGTA-456 manufacturing information and copies of any product related reports submitted to the FDA.
- All Study data shall be the sole property of the University of Minnesota. Magenta shall have the right, to use the Study data, for any purpose subject to any applicable signed informed consent documents and authorization forms.

If you decide to participate, some private health information about you will be stored in OnCore, the computer database at the Masonic Cancer Center. This information will include your name and medical record number, date of birth, diagnosis, race/ethnicity, and the type of transplant you have. The purpose of storing this information is to assist the Cancer Center in creating reports about research and in making sure that research studies are being done correctly. Your information will not be used for any other purpose. There are no plans to erase information from the database. It will be stored indefinitely at the Masonic Cancer Center.

Data or Specimens Collected

There may be some leftover blood cells from the samples collected for research purposes. With your permission; we would like to store them for up to 15 years after the study ends for future analysis as new research tests become available. These samples will be the property of the Blood and Marrow Transplant Program. The samples will not be used for studies other than ones to learn about the immune system and blood cancers.

The samples will be stored with indirect identifiers. They will be labeled with a unique code number, rather than a name or medical record number, and the samples can only be linked

back to the patient using a master list for the study. This master list will be kept in a secured manner and only accessible to persons directly involved with the research.

There will be no cost to you for storing and future testing of the leftover samples. You will not be paid for allowing your samples to be used for future research. Because it is not known how soon these samples will be used, you will not be given the results of the tests. Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the investigators will not contact you to let you know what they have found.

Fifteen years after the end of the study any remaining samples will be destroyed. However, if you agree to storage now and later change your mind, you may request to have any remaining identifiable samples destroyed by contacting the study doctor or another member of the study staff.

The sponsor, monitors, auditors, the IRB, the University of Minnesota Research Compliance Office and other University compliance units, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at 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.

Whom do I contact if I have questions, concerns or feedback about my experience?

This research has been reviewed and approved by an IRB within the Human Research Protections Program (HRPP). To share feedback privately with the HRPP about your research experience, call the Research Participants' Advocate Line at 612-625-1650 or go to https://research.umn.edu/units/hrpp/research-participants/questions-concerns. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.

- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

Will I have a chance to provide feedback after the study is over?

The HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous.

If you are not asked to complete a survey, but you would like to share feedback, please contact the study team or the HRPP. See the "Investigator Contact Information" of this form for study team contact information and "Whom do I contact if I have questions, concerns or feedback about my experience?" of this form for HRPP contact information.

What happens if I am injured while participating in this research?

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think that you have suffered a research related injury let the study physicians know right away.

Use of Identifiable Health Information

Your PHI created or received for the purposes of this study is protected under the federal regulation known as HIPAA. Refer to the attached HIPAA authorization for details concerning the use of this information.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

Yes, I agree	**No, I disagree**	
_____	_____	The investigator may retain any leftover blood samples taken during the study. These samples may be used for other research not related to this study. These samples will be retained in non-identifiable form, meaning that there will be no information associated with the blood samples that will allow anyone to readily ascertain my identity.
_____	_____	The investigator may retain any unusable product cells. These samples may be used for other research not related to this study. These samples will be retained in non-identifiable form, meaning that there will be no information associated with the cells that will allow anyone to readily ascertain my identity.

Signature Block for Capable Adult:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent

[Use if a witness will observe the consent process. e.g., participant is illiterate, participant physically unable to sign.]

WITNESS STATEMENT:
The participant was unable to read or sign this consent form because of the following reason:

☐ The participant is unable to read the information

☐ The participant is visually impaired

☐ The participant is non-English speaking

☐ The participant is physically unable to sign the consent form. Please describe:

_____

☐ Other *(please specify)*:

_____

For the Consent of Non-English Speaking Participants when an Interpreter is Used:
As someone who understands both English and the language spoken by the participant, I represent that the English version of the consent form was presented orally to the participant in the participant's own language, and that the participant was given the opportunity to ask questions.

_____ _____
Signature of Interpreter Date

_____
Printed Name of Interpreter

OR:

For the Consent of a Participant when a Non-Interpreter (General Witness) is Used:
As someone who understands both English and the language spoken by the participant, I represent that the English version of the consent form was presented orally to the participant in the participant's own language, and that the participant was given the opportunity to ask questions.

_____ _____
Signature of Witness Date

_____
Printed Name of Witness

Affix Patient Label Here

Signature Block for Adult Unable to Consent:

Your signature documents your permission for the named participant to take part in this research.

_____
Printed Name of Participant

_____ _____
Signature of Legally Authorized Representative Date

_____ _____
Printed Name of Legally Authorized Representative Date

_____ _____
Signature of Person Obtaining Consent Date

_____ _____
Printed Name of Person Obtaining Consent Date

Appendix

Study Calendar

Below is a calendar of standard of care study activities. This schedule is a common schedule for a patient having an umbilical cord transplant.

The following routine tests and evaluations may be done to determine if you can safely participate and in this study:

- Medical history and physical examination, including vital signs, height and weight
- Routine blood tests (requiring 2-3 tablespoons of blood) to evaluate hematologic, kidney, and liver function, as well as general health status
- Blood tests (requiring 1 tablespoon of blood) to check for exposure to hepatitis and HIV. If the results are positive, you will be notified and it will be recommended that a Blood Bank physician contact your personal physician regarding possible further testing. By law the Minnesota Department of Health must be notified if you test positive for hepatitis or HIV. Because of the sensitive nature of these tests, you have the right to review the results. If you test positive for some types of hepatitis or HIV, you will not be eligible for study.
- Urine test
- A pregnancy test (blood or urine) for women of childbearing potential.
- Tests to evaluate heart function including an electrocardiogram and an echocardiogram
- Chest x-ray
- Tests and procedures to evaluate your current disease status including a bone marrow biopsy
- Any additional tests or evaluations, felt necessary by the medical staff, to evaluate your current health

The **preparative regimen** is the chemotherapy and radiation that will be given to get your body ready to receive the transplanted cord blood. The same treatment will be given prior to the transplantation of expanded cord blood, referred to as MGTA-456.

Day	Preparative regimen	Supportive care therapy
-8	Fludarabine by IV over 1 hour	

-7	Fludarabine by IV over 1 hour Cyclophosphamide by IV over 2 hours	
-6	Fludarabine by IV over 1 hour Cyclophosphamide by IV over 2 hours	
-5	Rest	
-4	Radiation twice daily	
-3	Radiation twice daily	Begin Tacrolimus IV Begin MMF IV or pill
-2	Radiation twice daily	
-1	Radiation twice daily	
0	Cord blood infusion*	

*Prior to the infusion of the cord blood (in this case, MGTA-456), you will receive extra fluid and medications to prevent complications from the preservative used to freeze the cells. [Note: rather than the standard one bag of cord blood cells, you will receive 3 containing a total volume of about 6 ½ ounces.

Risks of Preparative Chemotherapy and Supportive Care:

Cyclophosphamide –

Common	Less Common	Rare, but may be serious
• low white blood cell count with increased risk of infection • hair loss or thinning, including face and body hair (usually grows back after treatment) • nausea • vomiting • loss of appetite • sores in mouth or on lips • bleeding from bladder, with blood in urine • diarrhea • long-term or short-term infertility (inability to have children) in women and men	• low platelet count (mild) with increased risk of bleeding • darkening of nail beds • acne • tiredness • infection • fetal changes if you become pregnant while taking cyclophosphamide	• heart problems with high doses, with chest pain, shortness of breath, or swollen feet • severe allergic reactions • skin rash • scarring of bladder • kidney damage (renal tubular necrosis) which can lead to kidney failure • heart damage, with trouble getting your breath, swelling of feet, rapid weight gain • scarring of lung tissue, with cough and shortness of breath • second cancer, which can happen years after taking this drug • death from infection, bleeding, heart failure, allergic reaction, or other causes

Fludarabine -

Common	Less Common	Rare, but may be serious
• low white blood cell count with	• pneumonia	• numbness and tingling in hands

increased risk of infection • low platelet count with increased risk of bleeding • low red blood cell count (anemia) with tiredness and weakness • tiredness (fatigue) • nausea • vomiting • fever and chills • infection	• diarrhea • loss of appetite • weakness • pain	and/or feet related to irritation of nerves • changes in vision • agitation • confusion • clumsiness • seizures • coma • cough • trouble breathing • intestinal bleeding • weakness • death due to effects on the brain, infection, bleeding, severe anemia, skin blistering, or other causes

Risks of Total Body Irradiation (TBI):

Total Body Irradiation		
Common	**Less Common**	**Rare, but may be serious**
• nausea and vomiting • diarrhea • cataracts • sterility (inability to have children) • endocrinopathies (hormone imbalance due to damage to the endocrine gland) • stunned growth in children • intestinal cramps • mucositis (mouth sores)	• parotitis (swelling and inflammation of the parotid gland) • interstitial pneumonitis (explained below in the damage to vital organs section) • generalized mild reddening of the skin • veno-occlusive disease (VOD - explained below in the damage to vital organs section)	• dysphagia (difficulty swallowing) • deformities of the backbone (vertebrae) • nephropathy (kidney disease or damage) • risk of 2nd malignancy years later (when given along with chemotherapy)

Cyclophosphamide and fludarabine are expected to cause transient marrow suppression (less than 2 weeks). Furthermore, the addition of TBI may increase the time duration of marrow suppression.

G-CSF (Given to Stimulate Bone Marrow and Blood Recovery):

common (occuring in 30 or more out of every 100 persons)	**less common** (occuring in fewer than 30 but more than 5 out of 100 persons)	**rare, but may be serious** (occuring in 5 or fewer out of 100 persons)
none	• bone or muscle pain • injection site reaction (redness, pain, or swelling)	• allergic reaction • spleen enlargement or rupture – symptoms of an enlarged spleen include a

common (occuring in 30 or more out of every 100 persons)	**less common** (occuring in fewer than 30 but more than 5 out of 100 persons)	**rare, but may be serious** (occuring in 5 or fewer out of 100 persons)
		feeling discomfort, fullness, or pain on the upper left side of the abdomen; this pain may spread to the left shoulder • serious lung problems (ARDS) • coughing up blood

Mycophenolate mofetil (MMF)

Common	**Less Common**	**Rare, but may be serious**
• miscarriage in pregnant women • birth defects • diarrhea • damage to unborn baby • limited effectiveness of birth control • stomach pain • upset stomach • vomiting • headache • tremors • low white blood cell count with increased risk of infection • increased blood cholesterols • swelling of the hands, feet, ankles or lower legs	• anemia • rash • difficulty falling asleep or staying asleep • dizziness • uncontrollable hand shakes	• difficulty breathing • unusual bruising • fast heartbeat • excessive tiredness • weakness • blood in stool • bloody vomit • change in vision • secondary cancers, such as lymphoproliferative disease or lymphoma • Progressive Multifocal Leukoencephalopathy – a very rare, but serious and often fatal inflammation of the brain

Tacrolimus		
Common	**Less Common**	**Rare, but may be serious**
▪ kidney problems ▪ loss of magnesium, calcium, potassium ▪ high blood pressure ▪ tremors ▪ increases in cholesterol and triglyceride	▪ nausea ▪ vomiting ▪ liver problems ▪ changes in how clearly one can think ▪ insomnia ▪ unwanted hair growth ▪ confusion	▪ seizures ▪ changes in vision ▪ dizziness ▪ red blood cell destruction

It is very important that grapefruit or drinks with grapefruit juice are not consumed while taking Tacrolimus. Grapefruit has an ingredient called bergamottin, which can affect some of the treatment drugs used in this study**.** Common soft drinks that have bergamottin are *Fresca*, *Squirt*, and *Sunny Delight*.

General Transplant Risks

The following problems may occur as a result of umbilical cord blood transplant; these are risks that would be present whether such a transplant was done as part of a study or not.

- **Slow bone marrow recovery (delayed engraftment).** Blood counts, including red blood cells, white blood cells, and platelets, may be very slow to recover after unrelated donor umbilical cord blood transplantation. Until the new cord blood stem cells begin to grow, you are at risk of developing infections or bleeding. Infections can be treated with antibiotics but sometimes can be very serious. Bleeding can be helped, at least in part, by transfusions. However, there are risks associated with the transfusion of red blood cells and platelets during the post-transplantation period.
- **Graft Failure.** Your body/existing blood cells may not accept the new cord blood stem cells and the blood cells do not recover which may be fatal. Experience suggests that this may occur in 8-15% of patients transplanted with cord blood that is not expanded. Low cell dose in the umbilical cord blood unit and HLA mismatch are risk factors for graft failure. It is possible that the cord blood stem cells will grow, but not work normally. This may result in low blood counts for a long period. Should the graft fail, you may be able to receive a second transplant with stem cells from another unrelated umbilical cord blood donor, unrelated adult volunteer donor or a mismatched parent, or sibling (i.e., brother or sister) donor.
- **Graft versus host disease (GVHD).** This complication results from a reaction of the transplanted umbilical cord blood cells against the body and organs. It may or may not occur more frequently in this trial. This reaction ranges from a mild skin disorder to severe involvement of the skin, liver, and/or gut. It may be fatal in some patients. You will be monitored closely for this complication and given specific treatment to prevent and treat it. There are 2 forms of GVHD: acute (early) and chronic (late) GVHD.

Acute GVHD may produce skin rashes, liver disease, diarrhea, and an increased risk of infection. All of these can range in severity from mild to fatal. To confirm the diagnosis of acute GVHD, you may be asked to have a skin biopsy (i.e., taking a piece of tissue to make the diagnosis of GVHD) and possibly a liver or gut biopsy. The treatment of acute GVHD may require you to take high doses of methylprednisolone or prednisone and, in some cases, other drugs such as ATG.

Chronic GVHD may produce skin rashes, hair loss, thickened skin, dry eyes, dry mouth, liver disease, diarrhea and an increased risk of infection. Chronic GVHD may be mild and respond to agents that suppress the immune system, or it could be very severe; it may also last for several years.

- **Genetic Disease Transmission.** It is possible that a genetic disease (such as thalassemia or Gaucher's disease) may be passed to you through the transplanted umbilical cord blood stem cells. Each umbilical cord blood unit can only be tested for a few of the many possible genetic diseases. We will obtain screening results from the cord blood banks for some of the common diseases, like thalassemia and sickle cell anemia. The family of each umbilical cord blood donor has been asked about known genetic diseases within the family to further reduce the possibility of genetic disease transmission (i.e., passage of a disease to you from the umbilical cord blood cells).

- **Incorrect Labeling of the UCB.** It is possible that an umbilical cord blood unit could be labeled incorrectly. Confirmation of tissue-typing will be performed on every unit by both the cord blood bank providing the umbilical cord blood unit and by our institution. Every attempt will be made to carry out confirmatory typing at this institution on all units before the transplant occurs, but this may not always be possible. Should the typing be incorrect and we detect the error, the transplant may be delayed until an alternative source of stem cells is located, which in this case would likely be a different umbilical cord blood unit or a mismatched related donor.

- **Disqualification of MGTA-456 for Transplant.** The cells grown in the laboratory may become contaminated or infected or not grow in culture at all. If so, these cells would not be safe for use. If this were to occur, you would receive a back-up umbilical cord blood transplant. A back up donor will be planned for in advance so that blood forming stem cells can be available quickly.

Other complications that can result from the transplantation procedure not specifically related to one specific drug, the umbilical cord blood stem cells or this study include:

- **Damage to the vital organs in the body.** This could result in malfunction of any organ in the body such as heart, lungs, liver, gut, kidneys and bladder, brain etc. The lungs and the liver are the most vulnerable. Some patients will experience severe lung problems due to infections and/or due to a reaction of the lungs to the conditioning regimen. Some patients can suffer veno-occlusive disease of the liver (VOD). Patients who have VOD become jaundiced (yellowish skin), have liver function abnormalities, abdominal swelling, and abdominal pain. Although

many patients recover completely, these complications may result in organ failure and permanent damage or even death.

- **Serious infections.** Full and complete recovery of the immune system may take many months following the initial recovery of your white cell count. During this time, there is an increased risk of infections including viral, bacterial or fungal infections. If you have an infection, you may have to stay in the hospital longer or be re-hospitalized after transplant. Infections can be fatal. The data collected from several transplant centers indicate that patients who have been exposed to a virus called cytomegalovirus ("CMV") prior to their cord blood transplant are at high risk of reactivating this virus after the transplant. CMV is a very common virus; it is estimated that about 50 to 80% of people have been exposed to CMV at some time in their life. In healthy people, the virus remains inactive and does not cause any harm. However, it often becomes reactivated in people with a weakened immune system, and it can cause serious disease in the lungs, digestive tract and other organs. Because cord blood transplant patients are at higher risk for reactivation of CMV, all cord blood transplant patients will be monitored very closely with a special blood test that can detect very early reactivation of CMV. If this test comes out positive, you will be given appropriate treatments to control the virus. This treatment can last for a long period of time in some patients.

- **Risk to the unborn Child if you are pregnant**. The treatments in this study have NOT been proven to be safe at any stage of pregnancy. Some are known to cause miscarriage and birth defects in women who become pregnant during or for some time after treatment. Therefore, if you are pregnant, intend to become pregnant, or are nursing, you are not eligible for this study. Females who have the potential of becoming pregnant must use a combination of two forms of effective birth control.

- **Sterility and Future Childbearing Potential for Men and Women**. The conditioning regimen for this study may affect fertility. Male patients may become sterile (unable to produce sperm). Female patients may find that their menstrual cycle becomes irregular or stops permanently. However, this DOES NOT MEAN THAT YOU CANNOT BECOME PREGNANT, and you must use two of the birth control methods listed above. Damage to reproductive tissue may result in a permanent inability to have a child or become pregnant. You should discuss these risks and options in detail with your doctor before entering this study.

- **Risk of the Central Venous Catheter**. The most common complications of catheters are clotting and local infection, which sometimes leads to a generalized infection in the blood. Clotting may require the catheter to be removed or treatment with a fibrinolytic agent (medicines that dissolve blood clots). Infections will be treated with antibiotics, and sometimes, removal of the catheter is required. Occasionally, skin redness at the catheter exit site occurs, which may require antibiotic treatment. There is also a small risk of puncturing the lung at the time of the catheter insertion. If this occurs, placement of a temporary chest tube to re-inflate the lung may be required. There are no long-term effects once the lung puncture has resolved.

- **Risk of blood and platelet transfusions**. Despite screening donors and testing, there remains a very low but real risk of infections from a blood transfusion. These include hepatitis, cytomegalovirus (CMV), and human immunodeficiency virus (HIV; the virus that causes AIDS) among others. In addition, transfusions can increase your risk of antibodies formed against blood and platelets, making it more difficult to find acceptable blood products. Transfusion reactions may occur. These may cause you to have itching, hives, swelling over parts of your body including inside your airway, which would make breathing difficult.

General Late Complications can be:

- Sterility (inability to have children)
- Hypothyroidism (poor function of the thyroid gland)
- Possible increased incidence of radiation or chemotherapy-induced cancer, or leukemia (rare)
- Possible brain injury (rare)

Appropriate monitoring for these and other side-effects will be done and treatment given as needed. Follow-up care in the hospital and later in the outpatient clinics will be necessary to observe your recovery and monitor for any possible late side-effects of your transplant.