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Masonic Cancer Center, University of Minnesota

Blood and Marrow Transplantation Program

CONSENT TO PARTICIPATE IN RESEARCH

CMV-MVA Triplex Vaccine to Enhance Adaptive NK Cell Reconstitution After Autologous Hematopoietic Cell Transplantation in Patients with Lymphoid Malignancies

Principal Investigator: Armin Rashidi MD, PhD

For questions about research appointments, the research study, research results, or other concerns, call the study team at: **Principal Investigator:** Armin Rashidi MD, PhD **Phone Number:** 612-625-9604 **Email Address:** arashidi@umn.edu	**If you need emergency care:** • Call 911 or go to your nearest emergency room right away. **If you do NOT need emergency care:** • Call or go to your regular doctor. It is important that you tell your regular doctor that you are participating in a research study. If possible, take a copy of this consent form with you when you go.

Supported By: This research is supported by The National Institute of Health. The study drug is supplied by City of Hope National Medical Center.

What is research?

Doctors and researchers are committed to your care and safety. There are important differences between research and treatment plans:

- The goal of research is to learn new things in order to help groups of people in the future. Researchers learn things by following the same plan with a number of participants, so they do not usually make changes to the plan for individual research participants. You, as an individual, may or may not be helped by volunteering for a research study.

- The goal of treatment is to help you get better or to improve your quality of life. Doctors can make changes to your treatment plan as needed.

What you should know about research studies:

- 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 are you being asked to take part in this research study?:

You are being asked to join this study because you have multiple myeloma or lymphoma and are planning to enroll on an autologous stem cell transplant study. .

Why this research is being done:

Although transplantation is a standard treatment for multiple myeloma and lymphoma, these diseases often relapse. Generally after transplant, patients are given a maintenance chemotherapy with the goal of prolonging remission/preventing relapse. The researchers on this study are looking at a way to prolong remission that uses your body's own immune system to fight the cancer.

Recently, researchers have found that a certain type of Natural Killer ("NK") cell in your body, called "adaptive NK cells" may lower the risk of relapse. These cells increase when exposed to the CMV virus. CMV is a type of virus that may be carried in an inactive state for life by some, but not all healthy individuals.

It has been observed that patients who have CMV activate after transplant have a lower risk of relapse. However, CMV poses its own set of risks, and we do not want patients to get a CMV infection in order to reduce the risk of relapse. Therefore we are researching whether giving patients a vaccination against CMV will activate the adaptive NK cells without activating the CMV virus.

The CMV vaccine tested in this clinical study has been developed at City of Hope National Medical Center and is called CMV-MVA Triplex ('Triplex'). Investigators have discovered that by placing 3 small pieces of CMV DNA (the chemical form of genes) into a very safe, weakened virus, the vaccine can induce immunity (the ability to recognize and respond to an infection) to CMV in animals. The viral vaccine used for this purpose is called "modified vaccinia Ankara" (MVA). The MVA virus cannot grow in humans and has a long record of safe use in people. Now MVA is being evaluated as a vaccine against several types of infections and cancer. Triplex was first tested in 24 healthy adults and appeared to be safe and to boost immunity to CMV, but it has not yet been approved by the Food and Drug Administration (FDA).

The purpose of this study is to see if the number of adaptive NK cells in your body increases after you receive two doses of the Triplex vaccine. We will also be looking at the overall instances of disease relapse and compare it to the number of patients who historically relapse after transplant.

How long will the research last?

We expect that you will be in this research study for one year.

How many people will be studied?

Twenty adult patients will be enrolled in this study.

What is involved in this study?

About a month before your scheduled transplant

The following routine tests and evaluations may be done to determine eligibility for this study:

- You will be asked about your medical history and have a physical examination
- You will also have about 2 tablespoons of blood drawn for routine blood tests
- If you are a woman, a blood (approximately 1 teaspoon) specimen will also be collected to perform a pregnancy test.

The results of these tests will determine whether you are eligible to begin the study treatment.

Study Procedures and Visits

On days 28 after your transplant procedure (HCT), your doctor will evaluate your health and confirm whether or not you can participate in the trial, depending on your health status.

You will receive up to two injections during your participation in the study. You will receive your first injection intramuscularly (IM) into the muscle of your upper arm on day 28 after transplantation. Prior to the second injection, your doctor will evaluate your health and confirm that you can receive the second injection. If eligible, you will receive your second injection IM on day 56 after transplantation. After each injection, you will be observed for 30 minutes. Also on day 56, you will have a tetanus vaccine (TDAP). We use the TDAP as a way to double check whether your body responds to vaccines in general.

If, based on your health status your doctor decides to discontinue a second vaccine injection on day 56, you will continue to receive clinical follow-up evaluations. You may also decide to continue having the scheduled blood draws for the study.

In addition to the vaccine, you will be required to have a minimum of 6 trial visits and 6 blood draws over 12 months. In general, at each study visit, about 4 tablespoons of blood will be drawn. The total amount of blood drawn for this trial will be about 24 tablespoons. The trial visits will coincide with your standard of care post-transplant visits, so you will not need to make an extra trip. Most of the blood draws to assess for your immune response are also part of routine monitoring of transplant patients. You will have:

- One screening visit
- A tetanus vaccine ("Tdap")
- Two Electrocardiograms (EKG). An EKG is a picture of the electrical action of your heart that requires attaching small pads (electrodes) to your skin. Although the previous trial with healthy adults using this vaccine did not report any damage to the heart, there is insufficient data at this time to confirm that this vaccine is non-toxic to the cardiovascular system. Therefore, EKG will be done twice during this study for safety monitoring.
- Six evaluation visits

All visits, blood draws and vaccine injections will be performed at a University of Minnesota clinic.

The table below shows when your visits will be scheduled and what will be done at each visit.

Study Day (in relation to transplant day 0)	**-30**	**+28**	**+56**	**+100**	**+180**	**+365**
Research Procedures: Screening Visit	X					
Triplex Vaccine		X	X			
Tetanus Vaccine			X			
Blood Draw	X	X	X	X	X	X
Pregnancy test*	X	X	X	X	X	X
EKG			X	X		
Standard of Care:						
Clinical Evaluation & Symptom Assessment	X	X	X	X	X	X
Clinical blood draw	X	X	X	X	X	X

***Only for females**

While you are in the study, you must:

- Follow the instructions you are given.
- Come to the study center for all visits with the study doctor.
- Give correct and accurate information about your medical history and current medical condition.
- Tell the study doctor about any health problems you have during the study.
- Tell the study doctor about any new medicine or drug you take during the study.
- Not take any other drugs or remedies unless the study doctor has approved them beforehand. This includes prescription drugs and over the counter medicine (including vitamins and herbal remedies) that you buy without a prescription.
- Not get pregnant or cause your partner to become pregnant
- Tell the study doctor or study staff if you want to stop being in the study at any time.

What are the risks of being in this study?

CMV-MVA Triplex vaccine: The vaccine has been administered to 24 healthy adults with minimal discomfort. Since this experimental vaccine has not been used in transplant recipients, you may experience side effects not seen in healthy research participants. Therefore, it is important that you report any side effects to the clinic staff as soon as they occur.

Initial Side Effects of the Injection:

As with all vaccines or drugs, you could have an allergic reaction such as a rash or hives. Allergic reactions can be dangerous; therefore the clinic staff will observe you for 30 minutes after each injection. None of the 24 healthy volunteers who received the Triplex vaccine had an allergic reaction to the vaccine. If you develop an allergic reaction, you will be given medication (Benadryl-like) to counter the reaction.

Later Side Effects:

Commonly reported side effects of the Triplex vaccine, occurring in about 1: 3 healthy volunteers were:

- pain, swelling, redness and itching at the injection site
- muscular aches
- chills
- headache
- tiredness

Less common side effects of the Triplex vaccine, occurring in less than 1:10 healthy volunteers were:

- cough
- nausea

These side effects do not generally last more than a few days and usually do not require treatment but you may be given other non-prescription analgesic medications (similar to aspirin) to help relieve the symptoms.

Long term risks:

Receiving this vaccine may prevent you from receiving investigational CMV vaccines at a later date. There is no approved CMV vaccine currently available.

Risks of a Vaccine Injection:

These side effects have been seen with other vaccines and could occur when you receive the Triplex vaccine, but they were not observed in the healthy volunteers vaccinated with CMV-MVA Triplex vaccine.

- developing a bruise at the site of injection
- infection
- hypotension (lowering of blood pressure).

Tetanus Vaccine: With any medicine, including vaccines, there is a chance of side effects. These are usually mild and go away on their own. Serious reactions are also possible but are rare. Most people who get Tdap vaccine do not have any problems with it. Common reactions include pain at the site of the injection, headache, body aches, and tiredness.

Blood Draws: Blood can usually be drawn from your central venous catheter at the time of the other blood draws required as part of your usual medical care. However, if it is not possible to draw blood from the central catheter, then it will be drawn from a vein. The needle used to draw blood from a vein may cause pain and bruising, and rarely, infection at the site of the blood draw. There is also a risk of anemia (low red blood cell count) or hypotension. Sometimes, having blood drawn will cause people to feel lightheaded or even to faint.

Electrocardiogram (EKG): Since EKG is done without entering the body and does not use dyes or x-rays, there is no pain or risk associated with having an EKG. You may have a mild rash where the electrodes (soft patches) were attached. This rash usually goes away without treatment.

Risk to an Unborn or Newborn Child: The effects of the trial vaccine on an unborn fetus or a newborn are unknown. If you are pregnant or breast-feeding, you cannot take part in this trial. Therefore, if you are a woman, you must have a negative pregnancy test at the screening visit and before each injection. If you become pregnant, you will receive no further injections. However, you will be asked to continue your trial follow-up visits.

If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study and for at least 90 days after the last vaccine, to avoid pregnancy. 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 may be required to stop participation in this study; however, other treatment options will be discussed with you at that time if necessary.

Benefits of Study Participation

If you agree to take part in this study, there may or may not be direct medical benefit to you. It is hoped the information learned from this study will benefit other being treated for multiple myeloma or lymphoma in the future.

Alternatives to being in this research:

The alternative to participating in this trial is not to participate. The purpose of this trial is research only and it is unknown whether receiving the investigational vaccine will affect the likelihood of a post-transplant disease relapse.

Leaving this research:

You can leave the research at any time. Leaving will not be held against you.

If you decide to leave the research, contact the investigator or study staff. A member of the study team may ask you some questions about being in the 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. Meaning, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.

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

Removal from Study:

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Even if you want to stay in the study, there may be reasons the study doctor or study staff will need to take you out of it. Your study doctor has the right to take you out of the study at any time with or without your agreement. Your participation may be

ended without your consent for different reasons, including the following:

- If the study doctor believes, for any reason, that it is in your best interest.
- If you develop side effects that the study doctor considers unacceptable.
- If you refuse to take the study drug or return for follow-up as recommended by your study doctor, or do not follow the study doctor's instructions.
- If you refuse to have tests that are needed to determine whether the study drug is safe and effective.
- If other causes prevent you from continuing in this study.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

Costs:
The investigational vaccine, Triplex, will be provided free of charge by City of Hope. Procedures that are not considered standard of care – the EKGs, post-transplant pregnancy testing, the TDAP vaccine, study-related blood draws – will be paid for by the study.

You will be responsible for all standard of care procedures (study visits on day 28, 56, 100, 180, and 360). Costs for standard of care procedures will be billed to you and/or your health insurance plan the usual way.

You will receive no payment or compensation for taking part in this study.

Research Related Injury:
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.

Confidentiality and Privacy:
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 privacy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution, including those that have responsibilities for monitoring or ensuring compliance.

- Every research site for this study, including the University of Minnesota, and each site's study team, research staff and medical staff.
- Any person who provides services or oversight responsibilities in connection with this study.

- Every 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)).
- National and international transplant registries including the Center for International Blood and Marrow Transplant Research (CIBMTR) and National Marrow Donor Program (NMDP)
- Other government agencies in this or other countries.
- The designated Protocol Review and Monitoring Committees, Institutional Review Boards such as the University of Minnesota IRB, Privacy Boards, Data and Safety Monitoring Board and their related staff that have oversight responsibilities for this study.
- The Masonic Cancer Center at the University of Minnesota and/or their designee
- The City of Hope National Medical Center, the maker of the study drug

If you decide to participate in this study, some private health information about you will be stored in a computer database at the University of Minnesota Masonic Cancer Center. This information will include your name and medical record number, date of birth, diagnosis, race/ethnicity, and information about your participation in this study. 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.

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.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it

illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Use of Identifiable Health Information

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission. Please read the HIPAA Authorization form that we have provided and discussed.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Contacts and Questions

This research has been reviewed and approved by an Institutional Review Board (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 www.irb.umn.edu/report.html. 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.

Feedback

After the study, you might be asked to complete a survey 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 after the study is over, but you would like to share feedback, please contact the study team or the Human Research Protection Program (HRPP). See the "Who Can I Talk To?" section of this form for study team and HRPP contact information.

Specimen Banking

With your permission, specimens left over after research tests listed above have been completed may be stored and used for future research purposes that have not yet been determined. Blood collected during the study may be stored at the University of Minnesota indefinitely. These samples may be used to develop new assay methods for testing samples from other subjects. In the event the samples are used for tests outside the scope of this study, they will be relabeled in an anonymous manner, so that you cannot be identified in any way. The scientific, diagnostic and/or medical significance of the research to be done is not known. Therefore, neither you nor your doctors will be informed of your individual results, and they will not affect your treatment in any way. Some of this research may result in new inventions or discoveries that may be of potential commercial value and may be patented and licensed for the development of new products. Donors of blood do not retain any property rights to the materials. Therefore, you would not share in any money or other benefits that any entity might receive for these inventions or discoveries. Your decision not to allow storage or future use of your tissue or specimens will not affect your ability to participate in this study.

If you agree to allow your specimens to be used for future research, you can change your mind later. Please initial below if you agree to have leftover specimens be stored for future research:

I agree to have my blood specimen stored for future research:

☐ Yes ☐ No *Initials*: _____

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