**DFCI IRB PROTOCOL NUMBER:** *02-100*

**PROTOCOL TITLE:** A Phase I Study Of Vaccination with Telomerase peptide plus GM-CSF

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**DFHCC SITE-RESPONSIBLE INVESTIGATOR(S)/INSTITUTION(S):** Dr. Nicholas Haining (DFCI/Children's Hospital – pediatric patients); Dr. George Demetri (Dana Farber Cancer Institute – adult patients); Dr. Tracy Batchelor(Massachusetts General Hospital)

# INTRODUCTION

You are being asked to take part in this research study because your have a type of cancer that is unlikely to be cured by current treatments (In this consent form "you" refers to the person who would be participating in the trial). This form was designed to help explain to you the nature of the research study we are inviting you to participate in. It's goal is to help you understand why this study is being done, what will be asked of you if you choose to participate, any possible risks, inconveniences or discomforts you may experience and other important information. This document is to be used as a guide for discussion between you and your physician. This form may also be helpful as a reference if you choose to participate, as a reminder of what your role in the study is, and who to contact if you have questions at any time during your participation. You are urged to discuss any questions you have about this study with members of the research team.

It is important that you read and understand several principles that apply to all people who participate in our studies. First, your participation is purely voluntary. Second, personal benefit may not result from taking part in this study, but knowledge may be gained that will help others in the future. Third, new findings relating to your treatment will be discussed with you. Fourth, you may withdraw from the study at any time, without affecting your care. If you do decide to stop participating in this study, we encourage you to discuss your decision with your doctor

# WHY IS THIS STUDY BEING DONE?

The main purpose of this study is to test the safety of a vaccine called Telomerase Peptide Vaccine, and determine the type and severity of any side effects associated with the vaccine. We will also be testing whether the vaccine boosts your body's ability to fight your cancer cells, and if the vaccine makes your tumor get smaller.
We hope that this vaccine will be able to help your immune system fight against your tumor cells. However, since this exact type of vaccine has not been given to people



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before, this study will test 1) whether it causes any side-effects in humans, and 2) how effective it is at generating an immune response before we will know whether it is able to treat your type of cancer.

# WHAT OTHER OPTIONS ARE THERE?

You should discuss other treatment options with your physician. If you choose not to take part in this study, your doctor may treat you with chemotherapy, radiation or other investigational agents. You may also decide to be treated not with the aim of getting rid of your cancer, but instead with the goal of keeping you comfortable.

# WHAT IS INVOLVED IN THE STUDY?

Before beginning this study, you will have blood tests (which require about 2 – 3 teaspoons of blood) and a physical examination to determine your general state of health. You may also have a scans of your tumor if they haven't been done in over a month. You will also have a "skin-test" which involves injecting small amounts of the vaccine to see if you have an immune reaction signaled by redness and swelling of the skin at that area.

The vaccine itself is given with a drug called Sargramostim (also called GM-CSF). Sargramostim is a drug that is routinely used by cancer patients to help boost white blood counts (cells that fight against disease) after chemotherapy, and also works to make vaccines more effective. The Sargramostim is given as an injection under the skin of the arm or leg every day for four days. On the third of the four days, the vaccine itself is given, also by an injection underneath the skin in approximately the same place as the Sargramostim was given. The Sargramostim can be given by nurses in clinic or at home. The vaccine will be given in clinic.

The vaccine is given every two weeks for three months and then every month for three months (nine vaccinations in total, over six months). During this time you will have frequent medical checks and blood tests to look for any signs of side-effects. We will also be taking blood tests (up to 3 tablespoons) seven days after each vaccine to see if you are making an immune response to it.

Every three months you will have another skin test using the vaccine. If there is redness or swelling around the skin test site, you will be asked to have a skin biopsy. This involves removing a tiny area of skin under local anesthetic. You will be asked for separate consent for that procedure.



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You will need to come into the clinic every week for three months (nine visits) and then twice a month thereafter as long as you are receiving vaccinations.

Every three months you will also have scans of your tumor to see if it has changed in size. Standard radiological testing (CT, MRI) will be used. The cumulative radiation exposure from these tests will not adversely affect your disease. The MRI scan will place you in a confined space, which may make you uncomfortable (Claustrophobic). The loud banging noises associated with MRI scans can be reduced with earplugs.

If samples of your tissue are ever removed by biopsy for other purposes (such as to help with diagnosis, or to relieve symptoms) we will study a portion of the tumor to see if there is any sign of immune reaction. You will not be asked to have a biopsy of your tumor just for the purpose of the research.

Approximately 35 patients will be involved in this study at the Dana-Farber Cancer Institute and Massachusetts General Hospital. These hospitals are the only locations where this study is being carried out.

# HOW LONG WILL I BE IN THE STUDY?

We plan to continue give you the nine vaccinations over six months. However, your participation may be shorter if 1) you no longer wish to take part in the research study; 2) you have concerning side-effects from the vaccine; or 3) your tumor gets bigger. The investigators and/or your doctors may decide to take you off this study without your consent if it is no longer in your best interest to continue, if the drug supply is insufficient, or if the course of your participation in this study is significantly different to that stated in the protocol.

# WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for the side effects described below. Since this is an investigational vaccine and it is the first time that this vaccine is being tested in humans, there may also be other side effects that we cannot predict. You may receive other drugs to makes side effects less serious and uncomfortable.

*Sargramostim (GM-CSF):* Side effects of this drug include

Common:

- fever



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- chills
- headache

Less common

- Redness, itching, swelling or discomfort at the injection site
- muscle and bone aches
- rash
- redness or swelling by injection site,

Uncommon

- nausea, vomiting, diarrhea,
- itching, swelling or retention of fluid.

*Vaccination*: The vaccination itself may cause redness, swelling or pain at the injection site. Based on similar vaccine studies, an immune reaction generated by the vaccine is unlikely to cause any side effects. However, because the protein that the vaccine targets is in some normal cells as well as your cancer cells, it is possible that normal tissues in your body may be damaged by the immune reaction against the vaccine. The tissues that express the protein include bone marrow cells and the cells that make blood cells; cells in your lymph nodes; and cells in your skin. Although damage to these tissues is unlikely, permanent, serious or even life-threatening side-effects could occur as a result of this vaccine.

The synthetic peptides used to make this vaccine are produced using a variety of materials some of which may have been derived from animal origin such as cows and sheep. Cows raised in some countries have had a fatal infectious disease known as Bovine Spongiform Encephalopathy (BSE). There are rare reports that people develop a fatal brain disease called new variant Creutzfeldt-Jakob Disease in countries where meat from infected cows was eaten. Symptoms of variant Creutzfeldt-Jakob Disease appear years after the people were probably exposed (ate infected meat). We do not know whether animal derived materials were used in making this vaccine. However, even if the materials used to make this vaccine came from countries where animals had BSE, the chance that you would develop variant Creutzfeldt-Jakob Disease is very small. If you have any concerns about the risk of variant Creutzfeldt-Jakob Disease you should discuss this with your doctor.

*Skin testing:* This may cause pain related to the needle-stick. Inflammation can arise at the site of the injection causing redness, swelling and pain.



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*Skin biopsy:* Those participants undergoing skin biopsy may experience minor bleeding redness and pain, and less likely, infection.

*Blood tests:* Blood tests are drawn to measure any immune reaction to the vaccine and to check for any signs of side-effects. Because blood samples are drawn frequently in this protocol, you may become mildly anemic. Some participants may even need blood transfusions to treat their anemia.

*Reproductive risks*: Because the drugs in this study can affect an unborn baby, you should not become pregnant or father a baby while on this study. You should also not nurse your babywhile on this study. If you have any questions about the reproductive issues or about preventing pregnancy, please discuss them with doctor.

In addition to the risks described in this section, as with all treatments, there may be side-effects that we do not yet know of. Such side-effects may be permanent, serious or life-threatening. Should any new side-effects become known that are significant, you will be told about them.

For your safety, please disclose to the study doctor all of your present and past diseases and allergies that you are aware of. Since the vaccine is new, its interactions with other drugs may increase your risk of side effects, or may still be unknown. It is important, therefore, that you share with the study doctor any prescriptions and/or over-the-counter drugs, herbal preparations, and nutritional supplements you are taking.

A significant risk of taking part in this study may be receiving a vaccine that is not effective in helping to treat your disease. This means that you may spend time and incur side effects from the vaccine that will not aid in the treatment of your disease.

## WHAT ARE THE BENEFITS OF THE STUDY?

We do not know if the vaccine will be useful in treating your tumor. Although some people who were treated with similar vaccines have had decreases in the size of their tumors, it is unlikely that this vaccine will cure you of your disease.

However, information that we learn from this research study will help in the design of more effective cancer treatments for patients in the future.

Information learned from your participation in this study, from tumor tissue or from blood tests may be used for research, teaching or for the development of new treatments or tests. Occasionally these form the basis for commercial products that may result in profits to the manufacturer or sponsor of these developments. There are no plans to reimburse you for any commercial developments arising from your participation.



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# WHAT ARE THE COSTS?

You will not be charged for the vaccine or for any of the research blood tests. However, the drug sargramostim (GM-CSF), physical examinations, radiological tests and other blood tests will be charged to you or your insurance carrier. Taking part in this study may lead to added costs to your or you insurance carrier. You should discuss any expected costs associated with this study or insurance problems with your doctor.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury

# HOW WILL MY PRIVACY BE PROTECTED?

You have a legal right to give or not give permission for others to have access to health information that can reveal your identity. Since you have a great deal of control over who can see and use this type of information, it is called "protected health information".

To do this research, we need to have access to some protected health information of study subjects. We will need to use it for research purposes, and release it to other people involved in the research or your routine health care. Therefore, in order for you to be in this study you will have to give us permission to collect certain health information about you and to use it and share it as is necessary to do this study.

**1. What protected health information will be collected, used and shared as part of this study?**

Your medical records may be reviewed. Researchers may also need to discuss your health care with your treating physician when it is appropriate to maintain the quality of your healthcare. We will also generate new health care information about you during the course of this study. This information will come from the tests and procedures and any interviews or questionnaires we are asking you to take while in the study. This will include your entire medical record., the results of the medical tests performed on you: bloodwork, radiology tests.



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Some information such as your name and medical record number will be kept but in a coded form and not attached to your name. We will store the code in a secure area and allow only the study team (the researchers, research nurses, and other study staff) to have access to this code. We will keep this code in order to maintain a link between your name and the information about you created and collected during this study. The coded information, without your name attached, may be shared with others outside the research.

**2. Why will my information be used and shared?**

The main reasons we will use and share your information are:

- to conduct and oversee the research study
- to make sure that this study meets legal, institutional, and accreditation requirements
- to conduct public health activities

Other reasons your information may be used and shared are for treatment, payment and health care operations. Medical information produced by this study may become part of your hospital medical record. In order to provide you with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department. Your hospital will provide you with more information about the collection and use of your information.

**3. Who will use or share the information about me that is collected by the research team?**

We will share your health information with people at the hospital who help with the research. We may share your information with other researchers outside of the hospital. We may also share your information with people outside of the hospital who are in charge of the research, pay for or work with us on the research study.

Your information may also be shared with members of the Institutional Review Board (IRB) and the Quality Assurance for Clinical Trials (QACT) office. These are the people who review and oversee research studies and study data to assure that the studies are safe and being well managed.

**4. With whom outside of the hospital may my information be shared?**

We will protect the information about you that we have access to, and will take care to maintain your privacy as much as possible. We may, however, need to share this information with the following people or groups so that they can carry out their duties related to this study:



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- The sponsor of this study and their clinical research organizations that manage the study
- The other hospitals and medical centers taking part in this study
- Federal Agencies, such as the Food and Drug Administration (the FDA), the Department of Health and Human Services (the DHHS), the National Cancer Institutes/National Institutes of Health (the NCI/NIH) and the Office for Human Research Protections (the OHRP)
- Hospital Accrediting Agencies
- Individuals or businesses outside the hospital that provide services, for example insurance companies, legal offices, and data storage companies
- The Data Safety Monitoring Board that oversees this study

Those who receive your information may share it if they are required to do so by law. These other groups may not be required to obey the federal privacy rules that the hospital and researchers must follow.

The results of this study may be published in a medical book or journal or used for teaching purposes. However, neither your name nor other identifiers will be used in any publication or teaching material without your specific permission.

## 5. How long will my information be used or shared?

If you sign this form, we will collect your health information until the end of the research. We may collect some information from your medical records even after your direct participation in the research project ends. We will keep all the information forever, in case we need to look at it again. We will protect the information and keep it confidential.

Your information may also be useful for other research studies. We can only use your protected health information again if a special committee in the hospital (the IRB) gives us permission. This committee may ask us to talk to you again before doing the research. But the committee may also let us do the research without talking to you again if we keep your health information confidential.

## 6. What are my privacy rights?

You have the right to withdraw your permission for the use your information. If you change your mind about taking part in this study, please contact us about your decision.



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We may still need to use the information we have already collected. It is often important to know what happened to everyone who starts a research study, not just those people who stay in it until the end. Once you withdraw your permission to participate in the study, no new information will be collected about you.

You have the right to access your information that is created or obtained during this research as it relates to your treatment or payment. You may access this information only after the analysis of the study is complete. To request this information you will need to contact the research team.

**7. Your Signature**

You have the right not to sign this form. If you do not sign the form, you cannot take part in this research study. However, this decision will not affect your relationship with the hospital, it will not affect your present or future health care, nor will it cause any penalty or loss of benefits to which you are otherwise entitled.

## WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

You are encouraged to ask questions about the study or your role as a participant at any time.
For questions about the study or a research-related injury, contact the investigators of this study

- Children's Hospital: Nicholas W. Haining, MD at 617-632-5293
- DFCI: George Demetri, MD at 617-632-3985
- MGH Tracy Batchelor, MD at 617-724-8770



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# Documentation of Consent

My signature below indicates my willingness to participate in this study and my understanding that I can withdraw at any time.

Subject Date

**Certification from person obtaining consent:**

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts as well as potential benefits and have answered any questions regarding the study to the best of my ability.

1. _____ I do not have a financial conflict of interest with this proposal.
2. _____I do have a financial conflict of interest with this proposal but it is within the de minimus as defined by the PHS guidelines (less than $10,000).

Signature of Person Obtaining Consent: _____
Printed Name of above: _____
Date:



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