PRINCIPAL INVESTIGATOR: **Hoyoung Maeng, M.D.**

STUDY TITLE: **A Randomized, Placebo-Controlled Phase II Study of Multi-Epitope TARP Peptide Autologous Dendritic Cell Vaccination in Men with Stage D0 Prostate Cancer**

STUDY SITE: **NIH Clinical Center**

Cohort: Affected patient

Consent Version: December 18, 2019

WHO DO YOU CONTACT ABOUT THIS STUDY?

PRINCIPAL INVESTIGATOR: Hoyoung Maeng, MD
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This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

IRB NUMBER: 15C0075
IRB APPROVAL DATE: 02/13/2020

WHY IS THIS STUDY BEING DONE?

Research has shown that men who continue to have an elevated or rising prostate specific antigen (PSA) level following their primary treatment for prostate cancer are at increased risk for their cancer to progress. PSA is a protein found on normal and cancerous prostate cells. PSA levels are used to identify men who are at increased risk for prostate cancer, to monitor disease progression, or to monitor responses to treatment.

The time it takes for the prostate cancer to progress can be highly variable- from months to many years. One measure that has been shown in studies to be accurate in predicting how quickly someone is likely to progress is based on the change in PSA levels over time. This is called the "**PSA doubling time**" (PSADT). Individuals that have a PSADT less than 3 months are more likely to experience disease progression, have lower survival rates and are not eligible for this study. In contrast, individuals that have a slow PSADT of greater than 15 months have an extremely low risk of death from prostate cancer; they are also not eligible for this study.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

We invite you to participate in this research study because you have D0 Prostate Cancer. D0 disease means that you continue to have elevated or rising levels of prostate specific antigen (PSA) in your blood following your initial treatment for your prostate cancer, even though there is no evidence that the prostate cancer has spread (or metastasized) to other organs in your body. Your PSADT is between 3 and 15 months, and you have met the eligibility criteria.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

A maximum of 75 total patients could be accrued to this study.

The initial accrual for this study will include a cohort of **6** patients to determine the preliminary safety of the multi-epitope (ME) TARP peptide vaccine. Once this preliminary safety is established, patients that subsequently enroll in the study will be randomized to receive either the ME TARP peptide autologous dendritic cell vaccine or an autologous elutriated monocyte placebo vaccine. Autologous means that the cells used to manufacture either the ME TARP dendritic cell vaccine or the elutriated monocyte placebo vaccine come from you (as opposed to cells from a related or unrelated donor).

DESCRIPTION OF RESEARCH STUDY

This is a Phase II clinical trial.

It is a blinded, prospective, randomized placebo-controlled study. Blinded means that you will not know whether you have been assigned to receive the active ME TARP vaccine or the inactive placebo vaccine. Both vaccines are made using immune cells collected from your own body. Randomized means that whether you are assigned to receive the active ME TARP vaccine or the inactive placebo vaccine occurs strictly by chance. This study involves a 2:1 randomization. The 2:1 randomization means that you have a two in three chance of being randomly selected to receive the active ME TARP vaccine instead of the placebo. The randomization assignment is generated by a computer and is not controlled by the Principal Investigator or any members of the protocol

research team. A placebo control is being used in this study because we are trying to determine if the responses we observed to the first TARP vaccine we tested can be confirmed.

The study is 96 weeks in duration.

Arm A: 44 patients will receive active, autologous ME TARP peptide DC vaccine

Arm B: 22 patients will receive *inactive*, autologous elutriated monocyte placebo vaccine

Vaccines will be administered intradermally (just under the top layer of the skin) at Weeks 3, 6, 9, 12, 15, and 24. See Study Chart.

Background

This Phase II study is a follow-up study to an initial first-in-human pilot study (NCI 09-C-0139) of a first-generation TARP peptide vaccine. TARP stands for T-cell receptor gamma Alternate Reading frame Protein. TARP is over-expressed in prostate cancer cells as well as in breast cancer and mesothelioma. The first-generation TARP peptide vaccine contained only two small pieces (peptides) of the TARP protein and could only be given to men with a certain tissue type. The second-generation vaccine platform being examined in this Phase II study is different in that it contains the original two peptides from the first-generation vaccine in addition to five new peptides for a total of seven peptides in the vaccine. Because the new peptides in this vaccine cover the entire TARP protein, there are additional targets for the immune system to respond to and the vaccine can be given to patients of all tissue types.

The 09-C-0139 NCI study fully enrolled 41 men with Stage D0 prostate cancer. Stage D0 means that the PSA has become detectable again or started to rise following primary treatment for prostate cancer, but there is no evidence by CT or bone scans that it has spread to any other organs in the body. In the 09-C-0139 study, TARP vaccination was found to be safe and well tolerated with side effects limited to local injection site reactions. In addition, three fourths of the men experienced a slowing in how fast their PSA was rising over time, known as PSA velocity. PSA velocity is commonly expressed by calculating the PSA Doubling Time or PSADT. In 09-C-0139 TARP vaccination was associated with an increase in the PSADT and a slowing in PSA velocity, meaning the PSA was not rising as quickly after TARP vaccination compared to patients pre-vaccine baseline.

The reason for this randomized phase II study of a second-generation TARP vaccine is to determine whether the effects on PSA velocity and slowing in how quickly the PSA was rising was a true, real effect due to the TARP vaccine and not just due to random chance.

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study you will need to have the screening examinations, tests or procedures to find out if you can be in the study. Some of these examinations, test or procedures may be repeated during the study to assure your safety and to assess your responses vaccination. Some of these screening tests may also be performed at your outside home institution. The examinations, tests, and procedures that are a part of the screening process include:

- Laboratory blood test such as CBC, Chemistries, Mineral, Hepatic, Acute Panel urinalysis and Thyroid Function Tests
- HLA, Lymphocyte subsets, PT/PTT, Amylase, Lipase, Lipid panel, PSA, TTV Viral screen, VDRL, Type and Cross
- As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will not be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.
- CT scan
- Bone scan
- Physical exam with past medical history
- Confirmation of prostate cancer

You will be asked to read and sign the informed consent, if we determine from screening that:

- You have met all eligibility criteria
- You have prostate cancer and an elevated or increasing PSA level following completion of primary treatment for your cancer.
- You have no evidence that the prostate cancer has spread to other organs in your body.
- You are not currently receiving androgen deprivation hormone therapy (prior therapy is allowed).
- You have a PSA doubling time (PSADT) between 3 and 15 months.
- You understand the informed consent

What happens next?

After you have been found eligible for the study, and you have signed the informed consent for this study you will be scheduled for an apheresis. Both Arm A and B will go through a 15-liter apheresis procedure. A large number of cells are required to ensure that we have sufficient cells to make your vaccines, whether you are receiving the active ME TARP vaccine or the inactive elutriated monocyte placebo vaccine. These cells are collected during the apheresis procedure. For those patients assigned to receive the elutriated monocyte inactive placebo vaccine, these cells would be available to make active vaccine in the event that significant slowing in PSA velocity is documented to occur with the active ME TARP dendritic cell vaccine. A description of the apheresis procedure is below. Apheresis may be required to be repeated during study participation if not enough cells have initially been obtained.

Apheresis

The procedure for obtaining certain types of blood cells through apheresis is a very common procedure that is done routinely here in the Clinical Center with very few risks. Apheresis requires you to have a needle placed in your arm where the blood can be removed from you and circulated through a cell separator machine (a machine that divides whole blood into red cells, plasma (the serum part) and white cells (that includes lymphocytes and monocytes). The white blood cells are

removed and the plasma and red cells are returned to you through another needle in your other arm. The procedure takes approximately 1 to 3 hours to complete. One of the purposes of this procedure is to allow the investigator to collect a sufficient number of immune cells to measure the immune response to the vaccine. This testing will provide no benefit to you and is part of the experimental portion of this research study. Patients do not need to be hospitalized for the procedure. The apheresis procedure will be done at the Department of Transfusion Medicine (Blood Bank) in the NIH Clinical Center and is carried out by trained nurses supervised by Blood Bank physicians.

Potential side effects associated with Apheresis: you may have some tingling in your face and lips due to the medicine used to keep your blood from clotting during the procedure. The nurses may give you calcium-containing tablets, such as TUMS, to chew that takes away this tingling. Some patients may feel faint or light-headed during or after this procedure. We ask that you make sure you have a good meal and are well hydrated prior to coming to the apheresis lab.

During the study

With each clinic visit you will have a physical exam, laboratory and research blood draws. You will be asked about any side effects or illnesses you may have had between visits. You will also be asked about your medications.

We will continue to monitor your PSA and calculate your PSA doubling time. You will continue to monitor your injection site and bring your Vaccine Report Card to your visits.

After the study

After you have completed the study, you will be contacted by phone, mail or through your local oncologist every year to see how you are doing for the rest of your life.

BIRTH CONTROL

If you are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment, and for 30 days after your last dose of vaccine. If you think your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- abstinence
- vasectomy

RISKS OR DISCOMFORTS OF PARTICIPATION

What side effects or risks can I expect from being in this study?

Everyone taking part in the study will be monitored very carefully for any side effects and we will ask you to fill out a Vaccine Report Card to monitor any symptoms you may have following your vaccine injection. Since we don't know all the side effects that may be associated with these

vaccines, it is very important that you report any changes that you may notice, even if your study team does not specifically ask about them.

In the NCI 09-C-0139 TARP vaccine study, the main side effects were limited to local injection site reactions that generally lasted about 5-7 days or less. The second generation ME TARP vaccine platform with multiple peptides that is being investigated in this study may result in more potent immune response with potentially more unexpected and unknown side effects such as:

- Fever
- Chills
- Rash
- Flu-like symptoms
- Headache

Likely

- Injection site reactions, including possible pain or soreness, swelling, itching, and/or redness at the injection site.

Less Likely

- It is possible that you could develop an immune response to the TARP peptide that will cause inflammation in your prostate gland if it was not taken out as part of the initial primary treatment for your prostate cancer. We did not observe this kind of inflammation in any of the men that received the TARP vaccine in the 09-C-0139 NCI study.
- More potent immune responses could also be associated with auto-immunity and inflammation of the thyroid gland. Although this was not observed in the 09C-0139 NCI study, your thyroid function will be monitored as part of this study.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

Taking part in this study may or may not provide a direct benefit to you. It is unknown whether vaccination with ME-TARP DCs will stimulate an immune response by your body.

Since this is an experimental therapy, no benefit can be promised. However, the information we obtain from both the laboratory studies and your response to vaccination may also allow us to advance the understanding and treatment of cancer vaccines for future patients.

ALTERNATIVE APPROACHES OR TREATMENTS

What other choices do I have if I do not take part in this study?

Treatment options for patients with elevated PSA levels but no evidence of disease spread to other organs following primary treatment for their prostate cancer includes watchful waiting or androgen deprivation hormone therapy. However, it is unclear for patients with this stage of disease (Stage D0) what the best approach is. Because many patients prefer to avoid the side effects of hormonal treatment (impotence, hot flashes, loss of libido, breast tenderness, osteoporosis and bone fractures) watchful waiting is often chosen.

If you develop evidence of disease progression, involving spread of your prostate cancer to the bone, brain or other organs, alternative treatments/therapy for your cancer may include:

- Getting treatment or care for your cancer without being in a study. Some examples include: treatment with hormone therapy, radiotherapy, chemotherapy or a combination of these approaches.
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.
- Taking part in another study.
- No further therapy at all.

Please discuss these options with your doctor.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if you your vaccine is delayed for more than 6 weeks
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if he/she decides to end the study

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

CONFLICT OF INTEREST

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

The National Institutes of Health and the research team for this study have developed a vaccine being used in this study. This means it is possible that the results of this study could lead to payments to NIH scientists and to the NIH. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from the development of multi-epitope TARP peptide vaccine.

The National Institutes of Health and the research team for this study are working in collaboration with PDS Biotechnology and with RareCyte, Inc. to perform tests on your samples. The companies also provide financial support for this study.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures performed outside the NIH Clinical Center, you may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor (Center for Cancer Research) or their agent(s).
- Qualified representatives from PDS Biotechnology and RareCyte, Inc., companies that will supply agents used to perform studies on your cells.

When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

If we share your specimens or data with other researchers, in most circumstances we will remove your identifiers before sharing your specimens or data. You should be aware that there is a slight possibility that someone could figure out the information is about you.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal

Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Hoyoung Maeng, M.D., 240-781-3253, Email: hoyoung.maeng@nih.gov. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only: This section is only required if you are doing the oral short-consent process and this English consent form has been approved by the IRB for use as the basis of translation.

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.