UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE

DIVISION OF ONCOLOGY TUMOR VACCINE GROUP

(TVG)

Consent to take part in a research study:

Supplemental HER2 CTL Peptide-Based Booster Vaccine Study

Principal Investigator
Mary L. Disis, M.D., Professor of Medicine: 206-616-1823

Emergency contact (24 hours)
Mary L. Disis, M.D.: 206-427-8700

WE INVITE YOU TO JOIN THIS RESEARCH STUDY. We would like to give you the option of receiving two booster vaccines.

You were previously enrolled in Phase I-II Study of Combination Immunotherapy for the Generation of HER-2/neu (HER2) Specific Cytotoxic T Cells (CTL) in vivo. We are interested in giving two booster vaccines along with PET scans and clinical/research blood monitoring to look at immune memory.

As you may recall, research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions. This consent form is to give you the information you will need to help you decide whether to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all of your questions, you can decide if you want to be in the study or not. This process is called 'informed consent.' We will give you a copy of this form for your records. The vaccine used in this study, which is the same vaccine you previously received, is not approved by the Food and Drug Administration (FDA) for commercial use; however, the FDA has permitted its use in this research study.

WHY ARE WE DOING THIS STUDY?

We would like to determine if adding booster vaccines will increase HER2 specific immunity and immune memory cells.

WHEN AND WHAT PROCEDURES AND TREATMENTS ARE INVOLVED IF YOU PARTICIPATE IN THIS STUDY?

If you decide to join this study, we will complete these tests and procedures:

<u>Booster Vaccine #1</u>

- Review and sign the consent form for the "Supplemental HER2 CTL Peptide-Based Booster Vaccine Study"
- Physical exam, vital signs, weight and a urine pregnancy test (if applicable):
  - If you are pregnant you will not be able to receive the study vaccine
- We will review your medications
- Blood tests:

- Complete Blood Count (CBC: white blood cells, red blood cells, platelets) and Comprehensive Metabolic Panel (CMP: sugar (glucose) level, electrolyte and fluid balance, kidney function, and liver function)
- Approximately half a cup of blood will be collected for research testing so we can measure your immunity before your first vaccine

➢ The study vaccine will be given under the skin (intradermally) on the arm or leg:
- One dose of the vaccine is given over several injections in the same general area as your previous vaccine(s)
- After you receive the study vaccine, we will watch you for a minimum of 60 minutes for any allergic-type reactions
    - Please allow time in your schedule for this 60 minute monitoring

<u>Approximately 48 hours after your first booster vaccine</u>
- ➢ You will need to return back to the medical center
- ➢ We will measure your injection site reaction
- ➢ Approximately half a cup of blood will be collected so we can measure your immune memory cells

<u>Booster Vaccine # 2 (6 months after your first booster vaccine)</u>
- ➢ Prior to your second booster vaccine you will receive a PET scan
- ➢ Physical exam, vital signs, weight and a urine pregnancy test (if applicable):
    - If you are pregnant you will not be able to receive any further vaccines
- ➢ We will review your medications for any changes
- ➢ Blood tests:
    - CBC, CMP
    - Approximately half a cup of blood will be collected for research testing so we can measure your immunity
- ➢ The booster vaccine will be given under the skin (intradermally) on the arm or leg
    - You will receive one dose of the vaccine given in several injections in the same general area
    - After you receive the study vaccine, we will watch you for a minimum of 60 minutes for any allergic-type reactions
        - Please allow time in your schedule for this 60 minute monitoring

<u>Approximately 48 hours after your second booster vaccine</u>
- ➢ You will need to return back to the medical center
- ➢ You will have a repeat PET scan to look for increased inflammation in your lymph nodes
- ➢ We will measure your injection site reaction
- ➢ Approximately half a cup of blood will be collected so we can measure your immune memory cells

<u>Six months after Booster Vaccine #2</u>
- ➢ Approximately one cup of blood will be collected for research testing so we can measure your immunity
    - Return to the UW Medical Center **<u>OR</u>**
    - Have the blood collected at your own clinic and shipped to us
    - If you choose to have the blood drawn at your own clinic we can pay for the blood collection kit and shipping costs, but the blood draw itself will be charged to either your insurance company or you

- Please check with your clinic in advance regarding costs to you

Long Term Follow-Up

- A request for records will be sent to your primary oncologist twice a year starting from your last visit for a total of 5 years. Information requested may include:
  - Recent lab results
  - Recent oncologist's notes
  - Imaging reports
- Notes will be reviewed by study team for any vaccine side effects and we may contact your oncologist if we have any concerns
- In addition, if you become pregnant after the study is over, please inform the study team

HOW LONG WILL YOU BE IN THIS STUDY?

If you join this study, it involves up to 5 visits over the total of 12 months. You would receive the booster vaccine 2 times during the entire 12 months of the study.

The study doctor or your doctor may take you off of the study treatment at any time. This would happen if:

- They think it is in your best interest not to continue in the study
- You are unable or unwilling to follow study procedures
- The whole study is stopped
- You want to enroll in another treatment trial
- You become pregnant
- You need to go on cytotoxic chemotherapy or any other medication that decreases your immune system
- If you need to take any systemic steroids (steroids by mouth or injection such as: prednisone, decadron, solu-medrol).

If you are thinking about dropping out of this study, please tell one of the study doctors or the research nurse. Contact telephone numbers for these people are located towards the end of this document.

If you leave the study, we will keep your tests results and information as part of the study records. We may ask you to undergo one final physical exam, which includes weight, vital signs, symptom assessment and blood collection, if applicable.

WHAT ARE THE SIDE EFFECTS (RISKS)?

In this part of the consent form, we tell you the side effects we expect from the procedures being done in this study. There may be side effects we do not know about yet. If we learn about other significant side effects, we will tell you. We carefully watch everyone in the study for side effects. If you want more information about side effects and risks, please ask the study doctor or research nurse.

You should talk to your study doctor about any side effects that you have while you are in this study.

Risks of Blood Tests

Likely >20%	Less likely ≤20%	Rare but serious <3%

Pain	Bruising Light-headedness Fatigue Fainting	Infection

Risk of Study Vaccines

Our group has given over 1100 vaccine injections in previous studies, and below are some possible risks:

Likely	Less likely	Rare but serious
Pain and discomfort during vaccine administration Redness and tenderness at injection site (this usually goes away in 1-2 days) Itching at vaccine site Fatigue Headache	Flu-like syndrome Muscle pain Nausea Chills Diarrhea	Allergic reaction, including shortness of breath, dizziness, a feeling of fainting, hives, and difficulty breathing caused by swelling of the mouth, face, tongue or throat Seizures Severe allergic reaction to the vaccine will require medication and may lead to hospitalization or death

Allergic Reaction Monitoring

Severe allergic reactions are not common, but they do occur. If they occur, they tend to happen within an hour or so of exposure to the substance causing the allergy. Because of this rare risk, we will watch you in the clinic for a minimum of one hour after you receive each vaccine and booster vaccine to make sure you have no immediate side effects or allergic reactions. We would be watching for shortness of breath, trouble breathing, hives, lightheadedness and give you medicine if needed. *Please allow time in your schedule for this 60 minute monitoring.*

Risk of Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF, Sargramostim)

GM-CSF is a natural substance that will be mixed and injected in very small amounts with the vaccine also known as an adjuvant. In our previous vaccine studies that used GM-CSF, patients sometimes complained of mild to moderate flu like symptoms (fever, chills, achiness, and fatigue) for 1 – 2 days after vaccination which may be related to the use of GM-CSF. The possible risks listed below are for a larger dose of GM-CSF than you will receive in this study; you will be getting a fraction of the regular GM-CSF dose.

Likely >20%	Less likely ≤20%	Rare but serious <3%
Local reactions at the site of injection Low grade fever (Less than 100.5° F) Chills Pain in the bones, muscles, chest, abdomen, or joints Nausea Vomiting Diarrhea Flu-like symptoms including fatigue, weakness, headache Decreased appetite Increased white blood cell count	Kidney and liver problems Rashes Liver enlargement Low blood pressure	Fluid retention (including fluid in lungs or around the heart) Blood clotting, including blood clots in the leg veins that can break loose and go to the lung Increased platelets, low albumin (a protein found in your blood), increase of liver enzymes Rapid or irregular heartbeat or other heart problems Allergic reaction, including shortness of breath, dizziness, a feeling of fainting, hives, and difficulty breathing caused by swelling of the mouth, face, tongue or throat Worsening of pre-existing fluid accumulation in arms and legs, in the lungs and around the heart that may result in breathing problems and heart failure Neurologic syndrome called Guillain-Barré syndrome, where a person's own immune system damages their nerve cells, causing muscle weakness and sometimes paralysis Temporary loss of consciousness

***Liver enlargement is serious and may lead to life threatening complications.**

PET Scan

There are some risks from the PET scan used to monitor your response to treatment. This scan will expose you to radiation. If you live in the US, you receive about 3 millisieverts of radiation each year. It comes from space and the earth around you. This is called "background radiation." A "millisievert" (mSv) is a unit used to measure doses of radiation. The radiation dose to your whole body is:

- PET scan: 6 mSv

The risk of harm from this amount of radiation is low. If you have more procedures that expose you to radiation, this risk will go up.

Reproductive Risks

- Women should not become pregnant
- You should not nurse a baby after enrolling into this study

- For both women and men who are having sex that could lead to pregnancy, you must agree to use contraception for the remainder of your childbearing years
  - Check with a study doctor about birth control methods, some common methods might not be appropriate
- There may be long term effects on fetal tissue that we are not aware of

WHAT ARE THE BENEFITS?

It is possible that there may be no benefits to you as a result of receiving these booster vaccines, but future patients with breast cancer may benefit from your participation in this study.

YOU HAVE OTHER CHOICES BESIDES THIS STUDY.

Each of these choices has risks and benefits. You do not have to join this study. You are free to say yes or no. Your regular medical care will not change. If you do not join this study, you have other choices for treatment. Talk to your doctor about your choices, which may include:

- Another research treatment
- Standard treatment
- No treatment
- Other immune based treatment

PROTECTING YOUR PRIVACY AS AN INDIVIDUAL AND THE CONFIDENTIALITY OF YOUR PERSONAL INFORMATION

Some people or organizations may need to look at your records for research, quality assurance, or data analysis. They include:

- Researchers involved with this study
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB An IRB is a group that reviews the study to protect your rights as a research participant:
- Fred Hutchinson Cancer Research Center, University of Washington, and Seattle Cancer Care Alliance
- Food and Drug Administration (FDA)
- Office for Human Research Protections (OHRP)

We will do our best to keep your personal information confidential, but we cannot guarantee total confidentiality. Personal information is information that can identify you (name, date of birth, or other information). Your information will be locked in secured filing cabinets and a password protected computer. Your sample(s) will be assigned a unique identification number that will contain no personal identifying information.

Study charts are kept for 30 years after the close of the study per University of Washington policy. In addition, the University of Washington has a secure facility where research documents can be stored.

Documents, that could include personal information, may be given out if required by law. We may contact your physician regarding your study treatment. We will not use your personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

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

In the future if you give permission to any person or group to look at your medical record (such as an insurance company or employer) they could receive this research information. If you have already given permission to anyone (such as your life or health insurance company) to look at your medical record, they may receive this information if they ask for a copy of your medical record.

WOULD WE PAY YOU TO BE IN THIS STUDY?

There is no payment for being in this study. You will be given the option of receiving pre-paid parking vouchers for your research visits to the University of Washington Medical Center.

WOULD YOU HAVE EXTRA COSTS IF YOU JOIN THIS STUDY?

There is no charge for the medical costs directly related to the clinical testing (physical exam, PET scans) and laboratory testing (blood draws) done as part of this study. The costs related to the preparation and administration of the vaccine will also be provided.

WHAT IF YOU GET SICK OR HURT AFTER YOU JOIN THIS STUDY?

For a life threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact Mary L. (Nora) Disis, 206-427-8700. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

STORING SAMPLES FOR FUTURE TESTING

After we complete the research procedures on your specimens for this study there may be some specimens left over. We would like you to donate any leftover specimens for future research to the repository that the Tumor Vaccine Group (TVG) has. This future research may relate to immune response tests, or development of vaccines or other immunotherapies. You will be asked to sign a separate consent form for this purpose.

YOUR RIGHTS

- If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.
- Once you received the study vaccine (one or more), it may remain in your body permanently. You may continue to have the same side effects that you had while on study or experience new ones. If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.

- During the study, we may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you change your mind about being in this study. If we learn these kinds of information, we will tell you.

FOR MORE INFORMATION

If you have questions or concerns about this study, you may talk to your study doctor anytime. Other people you can talk to are listed below:

If you have questions about:	Call:
This study (including complaints and requests for information)	Dr. Mary Disis: (206) 616-1823 Doreen Higgins: (206) 616-9538
If you get sick or hurt in this study	Dr. Mary Disis pager: (206) 427-8700
Your rights as a research participant	Karen Hansen (206) 667-4867 (Director of Institutional Review Office, Fred Hutchinson Cancer Research Center) Karen Moe (206) 543-0098 Human Subjects Division, University of Washington)

Emergency number (24 hours): (206) 427-8700

YOUR RESPONSIBILITIES

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Prevent pregnancy.
- Tell us about side effects.

SIGNATURES

If you have read this form (or had it read to you), have had a chance to ask questions, and agree to participate, please sign:

_____	_____	_____	_____
Signature of Participant	Date	Time	Printed Name of Participant

Is it OK if someone from the Tumor Vaccine Group contacts you in the future regarding this or other TVG research?
(Circle one)

YES NO Initials: Date:

RESEARCHER'S STATEMENT

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

_____	_____	_____	_____
Signature of Researcher	Date	Time	Printed Name of Researcher

SCHEDULE OF EVENTS

Visit Time Point	Procedures
Booster Vaccine #1	• **Informed Consent** • **Medical history and complete physical examination** • **Vitals signs-including weight** • **Urine pregnancy test if applicable** • **Clinical labs: complete blood counts, serum chemistries** • **Research blood: approximately half a cup** • **Symptom assessment** • **Booster vaccine #1** • **60 minute post vaccine monitoring**
Approximately 48 hours after Booster Vaccine #1	• **Measure vaccine site** • **Research blood: approximately half a cup**
Booster Vaccine #2: **Six months post first booster vaccine**	• **PET scan prior to the vaccine** • **Complete physical examination** • **Vitals signs-including weight** • **Urine pregnancy test if applicable** • **Clinical labs: complete blood counts, serum chemistries** • **Research blood: approximately half a cup** • **Symptom/toxicity assessment** • **Booster vaccine #2** • **60 minute post vaccine monitoring**
Approximately 48 hours after Booster Vaccine #2	• **Measure vaccine site** • **Research blood: approximately half a cup** • **PET scan**
Six months after Booster Vaccine #2	• **Research blood: approximately one cup***
Long-Term Follow-Up for 5 years	• **Every 6 months for 5 years** • **Medical documentation request of your oncologist**
During the consent process, and at subsequent visits, patients will be instructed to hydrate sufficiently prior to visits requiring large volume blood draws. ***If research blood is drawn at the patient's own clinic, we will pay for the blood collection kits and shipping costs, but the blood draw itself will be at the patient's expense.***	