Official Title	A Phase II Randomized Study of Safety and Efficacy of a Multiple Antigen Vaccine (STEMVAC) in Non-Small-Cell Lung Cancer Patients
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UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE
DIVISION OF ONCOLOGY
CANCER VACCINE INSTITUTE (CVI)
Fred Hutch (FH)

Consent to take part in a research study:

A Phase II Randomized Study of Safety and Efficacy of a Multiple Antigen Vaccine (STEMVAC) in Non-Small-Cell Lung Cancer Patients

PRINCIPAL INVESTIGATOR:
Shaveta Vinayak, MD, University of Washington, (206) 616-0583
Co-Principal Investigator: Rafael Santana-Davila, M.D. University of Washington, (206) 606-2048

EMERGENCY NUMBER (24 hours):
Rafael Santana-Davila, M.D., University of Washington, or Hematology-Oncology Fellow on-call 206-598-6100 (24-hour number)

Important things to know about this study.

Your doctors are inviting you to participate in a research study. The purpose of this research is to examine if giving a vaccine, called STEMVAC, to you while you are on maintenance therapy for non-small cell lung cancer (NSCLC) will activate certain immune cells to recognize and kill lung cancer cells.

New therapies that involve the immune system, such as vaccines, are being evaluated to determine if they can help to fight cancer like advanced non-small cell lung cancer.

STEMVAC vaccine, targets 5 proteins that are expressed in lung cancer cells and are important for the tumor growth.

Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) is a protein that the body makes to increase immune cells in the bone marrow and activate the immune system.

The STEMVAC vaccine is given with GM-CSF which is being used as an adjuvant to help create a stronger immune response.

If you are eligible and agree to join the study, you will be enrolled and randomly assigned in equal numbers to one of two treatment arms (20 patients per arm) as follows:

Arm 1: STEMVAC vaccine (300 mcg) mixed with GM-CSF (100 mcg)

Arm 2: GM-CSF (100 mcg) alone

You will continue receiving pemetrexed/pembrolizumab (per standard of care) with your primary oncologist; this will not be provided by the study.

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There will be up to four treatment visits, two biopsies, up to a cup of blood drawn up to four times to look for immune cells, and two CT scans (per standard of care), over approximately 5 months.

We do not know if giving either the vaccine STEMVAC with GM-CSF and/or GM-CSF alone, with your maintenance therapy will help fight your lung cancer, and they could even make your condition worse. Both treatments (STEMVAC vaccine with GM-CSF or GM-CSF alone) could cause side effects such as pain or redness at the injection site, headaches, and fatigue.

You do not have to join this study. You could choose to receive standard methods to treat your cancer instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

The following is a more complete description of this study. Please read this description carefully. Afterwards, you can ask questions that will help you decide whether to join the study. If you join this study, we would give you a signed copy of this form to keep for future reference.

The Department of Defense (DOD) is a funder and Sponsor of this study.

We invite you to join this research study.

We invite you to join this research study because you have stage 4 NSCLC.

Research is not the same as treatment or medical care. The purpose of a research study is to answer specific questions.

You do not have to be in the study. You are free to say “yes” or “no”, or to drop out after joining. If you say “no,” you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?

We are doing this study to examine if giving the STEMVAC vaccine mixed with GM-CSF or GM-CSF alone will activate certain immune cells that will fight your cancer. Vaccines work by boosting the immune system to recognize and destroy the invader that is causing the disease. You have completed 3 - 4 cycles of chemoimmunotherapy, (induction treatment), and are receiving or will be receiving maintenance therapy with pembrolizumab with or without pemetrexed. We are studying if activating certain immune cells with vaccination will give you a good response to your treatment.

The STEMVAC vaccine is made up of DNA, which is a natural substance in every living organism. DNA acts like a blueprint that tells all the cells in your body how to function. The DNA we are using in this study contains instructions for your body to produce parts of the 5 proteins we identified (CDH3, CD105, YB-1, MDM2 and SOX2).

GM-CSF is a protein that activates and communicates with specific immune cells (T-cells, macrophages and dendritic cells) to increase immune response. GM-CSF, also called Sargramostim, rhuGM-CSF or Leukine, is a man-made protein that is almost identical to a protein the body makes. GM-SCF is an approved drug commonly used to support the recovery of immune cells after chemotherapy or bone marrow transplantation.

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The purpose of this study is to determine whether STEMVAC vaccine + GM-CSF or GM-CSF alone increases the traffic of immune cells to the tumor and if they can eliminate cancer cells. This will be evaluated in two core needle biopsies by comparing the number of immune cells and cancer cells in the biopsy before and after treatment with STEMVAC vaccine + GM-CSF or GM-CSF alone. The blood drawn will be used to determine the strength of the immune response generated against the tumor proteins included in STEMVAC vaccine. In this study, we also want to learn what effects, good or bad, the STEMVAC vaccine has on patients who are on pembrolizumab with or without. If you join this study, we watch carefully for any side effects.

What research tests, procedures, and treatments are done in this study?

All vaccine visits are outpatient and will be at the University of Washington Translational Research Unit (UW TRU), with the biopsies being done at either University of Washington Medical Center or Fred Hutch Cancer Center. If you need to receive a COVID-19 vaccine or any other non-study related vaccine during the study, you need to allow at least 14 days between the non-study related vaccine dose and any scheduled experimental treatment administration.

If you join this study, we would do these tests and procedures:

Baseline evaluation – some of these procedures may be done up to 60 days before your first treatment visit:

- Informed consent conference. Review consent and have all your questions answered so you can make an informed decision to join the study or not.
- Tumor imaging – CT or MRI/CT (per standard of care) if not completed within 60 days of first treatment.
- Review your medical history and ensure you meet the eligibility criteria.
- CT or ultrasound guided core biopsy of tumor – to be done prior to receiving first treatment (archived tissue may be used at the discretion of the study principal investigator provided there is sufficient tissue to evaluate).
- Physical exam which includes vital signs and weight.
- Medication review.
- Urine pregnancy test if applicable.
- Clinical blood draw:
    - Routine blood tests to evaluate kidney, liver, and blood system function (CBC-complete blood count w/ differential and CMP-comprehensive metabolic panel).
    - Immunotherapy labs: ANA, C3, anti-dsDNA, and thyroid function test.

First treatment visit

- STEMVAC vaccine + GM-CSF or GM-CSF alone administered 14 days (+ 3 days)* after your maintenance infusion of pembrolizumab with or without pemetrexed (administered by your treating physician under local procedures).

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- We may use the clinical labs and physician exam that was done during the baseline evaluation visit.
- Urine pregnancy test if applicable.
- Tetanus diphtheria vaccination if you have not had one in the last 6 months. This will help us measure your overall immune response. If you have had an allergic reaction to tetanus in the past, you do not have to have this vaccination.
- Research blood draw.
    - Approximately one cup of blood will be collected for research testing so we can measure your immunity.
- Treatment 1: STEMVAC vaccine (300 mcg) + GM-CSF (100 mcg) or GM-CSF (100 mcg) alone.
    - The treatment is given intradermal (under the skin) in your upper arm area.
    - The inoculation dose will be given in two or three injections. This is based on the lot of vaccine you should receive; the lots are both STEMVAC made from the same components.
    - You will need to stay at the clinic for at least 60 minutes after the treatment for observation of any allergic reaction.
        - Please build this into your schedule.

Second Treatment

- STEMVAC vaccine + GM-CSF or GM-CSF alone 14 days (+ 3 days)* after your maintenance/standard therapy.
- Complete physical examination.
    - Vitals signs-including weight.
    - Assess for any side effects.
- Urine pregnancy test (if applicable).
- Clinical labs.
    - CBC and CMP.
    - ANA, C3, anti-dsDNA, thyroid function test.
- Treatment 2 (*STEMVAC vaccine + GM-CSF or GM-CSF alone*).
    - Given intradermal in the same area as your previous vaccine.
    - Inoculation dose will be given in two or three injections.
    - After treatment monitoring for allergic reaction for a minimum of one hour.
        - Please build this into your schedule.

Third Treatment

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- STEMVAC vaccine + GM-CSF or GM-CSF alone 14 days (+ 3 days)* after your maintenance therapy.
- Complete physical examination.
  - Vitals signs-including weight.
  - Assess for any side effects.
- Urine pregnancy test (if applicable).
- Clinical labs.
  - CBC and CMP.
  - ANA, C3, anti-dsDNA, thyroid function test.
- Treatment 3 (*STEMVAC vaccine + GM-CSF or GM-CSF alone*).
  - Given intradermal in the same area as your previous vaccine.
  - Inoculation dose will be given in two or three injections.
  - After treatment monitoring for allergic reaction for a minimum of one hour.
    - Please build this into your schedule.

Evaluation #1 – after 3rd treatment

At least 3 weeks after your third treatment.

- Complete physical examination.
  - Vitals signs-including weight.
  - Assess for any side effects.
- Clinical labs.
  - CBC and CMP.
  - ANA, C3, anti-dsDNA, thyroid function test.
- Research blood draw.
  - Approximately one cup of blood will be collected for research testing so we can measure your immunity.
- CT or ultrasound guided core biopsy of your tumor.
- Tumor imaging – CT or MRI/CT (per standard of care).

Evaluation #2/Booster Treatment

STEMVAC vaccine + GM-CSF or GM-CSF alone at least 9 weeks after your third treatment and 14 days (+ 3 days)* after your maintenance/standard therapy.

- Complete physical examination.
  - Vitals signs-including weight.
  - Assess for any side effects.

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- Urine pregnancy test if applicable.
- Clinical labs.
    - CBC and CMP.
    - ANA, C3, anti-dsDNA, thyroid function test.
- Research blood draw.
    - Approximately one cup of blood will be collected for research testing so we can measure your immunity.
- If still on study treatment: STEMVAC vaccine (300 mcg) + GM-CSF (100 mcg) or the GM-CSF (100 mcg) vaccine only.
    - The treatment is given intradermal (under the skin) in the same area as your previous vaccines.
    - Inoculation dose will be given in two or three injections.
    - You will need to stay at the clinic for at least 60 minutes after the treatment for observation of any allergic reaction.
        - Please build this into your schedule.

Post booster treatment evaluation if applicable

At least three weeks after your booster.

- Complete physical examination.
    - Vitals signs-including weight.
    - Assess for any side effects.
- Clinical labs.
    - CBC and CMP.
    - ANA, C3, anti-dsDNA, thyroid function test.
- Research blood draw.
    - Approximately one cup of blood will be collected for research testing so we can measure your immunity.

(*) If your maintenance therapy is delayed, the experimental treatment may be delayed, with study team approval. If your maintenance therapy is changed, changes will be discussed with the study team concerning your treatment administration.

How long would you stay in this study?

If you join this study, you could have study visits for approximately 5 months.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.

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- Confirmed radiographic disease progression (patients with disease progression may continue study drug per discretion of PI).
- Another illness that prevents further infusions.
- Unacceptable side effects.
- You become pregnant.
- The whole study is stopped.
- We lose contact with you.
- Taking certain medications for a prolonged period of time (i.e. systemic steroids, supplements, etc.). Systemic steroids should not be taken for 7 or more days.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

Long-term Follow-up

Twice yearly for 5 years.

Long-term follow-up means keeping track of someone's medical condition for a long time. We would ask your doctor to send a copy of your medical records. This information will help us learn about the long-term side effects of the STEMVAC vaccine with your maintenance therapy.

You do not have to be in long-term follow-up. You could say "yes" or "no". Either way, you could still join this study.

If you chose not to join long-term follow-up, we would not ask your doctor to send medical records, but we might still need to contact you for some other reason.

There is a schedule of these events included at the end of this consent form.

What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. The combination of the treatment (STEMVAC vaccine mixed with GM-CSF or GM-CSF alone) and the maintenance therapy could cause side effects we do not know about yet. We carefully watch everyone in the study for side effects.

You are on three medications that are considered standard of care. We do not know what the interactions between STEMVAC vaccine + GM-CSF or GM-CSF alone and your standard medications will be. Please contact your study doctor if you experience additional side effects or have questions.

If you join this study, we would tell you if we discover new side effects that could affect you.

This form lists side effects of *individual* STEMVAC vaccine. Side effects that are common to both STEMVAC vaccine and your maintenance therapy appear in **bold**. Their incidence may increase when the drugs are used together.

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Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Many side effects go away soon after you stop treatment. In some cases, side effects can last a long time or never go away.

STEMVAC Vaccine

STEMVAC vaccine mixed with GM-CSF has been administered in an early phase (Phase 1 study) in 32 patients.

Possible side effects are below.

Likely	Less Likely	Rare, some may be serious
Pain and discomfort during STEMVAC vaccine administration Redness and tenderness at injection site (this usually goes away in 1-2 days) Itching at vaccine site **Fatigue**[a, b] Headache	Flu-like symptoms Muscle pain **Nausea**[a, b] Chills **Diarrhea**[a, b]	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 STEMVAC vaccine may require medication, lead to hospitalization, and may result in death

[a] Also common and expected in pemetrexed and/or pembrolizumab.
[b] Also common and expected with pembrolizumab

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Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF)

Possible side effects are below.

Likely	Less likely	Rare, some may be serious
Local reactions at the site of the injection **Low grade fever (< 100.5°F)** [a, b] Chills Pain in the bones, muscles, chest, abdomen, chest, or joints **Nausea** [a, b] **Vomiting** [a, b] Diarrhea Flu-like symptoms including **fatigue**[a], weakness, headache **Decreased appetite** [a, b] Increased white blood cell count	Kidney and liver problems Local reaction at the site of injection 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, 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 Temporary loss of consciousness

[a] Also common and expected in pemetrexed and/or pembrolizumab.
[b] Also common and expected with pembrolizumab

Allergic Reaction

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 treatment 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.*

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Blood Tests

About 1 cup of blood will be drawn before the first treatment and again approximately 3 and 9 weeks after the third treatment and 3 weeks after the booster treatment. It is possible that this volume of blood loss could cause you to feel lightheaded or dizzy. It is important to drink lots of water prior to these visits so that you are well hydrated for the blood draws, which may help to prevent these symptoms. If you experience lightheadedness or dizziness following your blood draw, the study doctor may give you IV fluids that will help relieve these symptoms.

Likely >20%	Less likely ≤20%	Rare but serious, <3%
Pain	Bruising Light-headedness Fatigue Fainting	Infection

Tetanus Diphtheria Immunization

Likely >20%	Less likely ≤20%	Rare but serious, <3%
Redness, pain and swelling at site Mild fever Decreased appetite	Hard lump at the site Allergic reactions such as: hives, rash, and itching Fever	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 Severe allergic reaction to the Tetanus Diphtheria vaccine may require medication or lead to hospitalization or death

Biopsies

You will be asked to have two core needle biopsies, one at the start of the study before receiving the vaccine so that your study doctor may determine the effects of the study drug on your disease. You will be given a separate surgical consent form for this hospital procedure. In a core needle biopsy, a small needle is used to remove a small cylinder (about 1/16 inch in diameter and 1/2 inch long) of tumor tissue. Core needle biopsies are usually done with local anesthesia in the doctor's office or clinic. The last decision on the site for the biopsy will be made by the radiologist performing the biopsy. The radiologist will decide the biopsy site based on patient safety.

Biopsy procedures may be associated with pain, discomfort, bleeding, swelling, scarring, bruising, and infection. To reduce these risks, the site of the biopsy will be numbed and sterile techniques will be used.

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The costs of the biopsies are covered by this study.

Radiation Exposure (CT scan)

These procedures most likely be performed per standard of care. Some of the tests that you will have in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called “background radiation”. This radiation is natural and comes from space, air, water, soil, and the food you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. For comparison, the estimated radiation dose from each of these tests is listed below. The risk to your health from this level of radiation exposure is too low to be detectable and may be nonexistent.

- CT scan of head: 2 mSv
- CT chest: 7mSv
- CT abdomen: 8 mSv
- CT pelvis: 6 mSv

Reproductive Risks

Taking STEMVAC vaccine mixed with GM-CSF or the GM-CSF alone with your maintenance therapy may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant. Therefore, you could not join this study if you are pregnant, if you are planning to become pregnant, or if you are breast-feeding.

If you join this study, you would have to use an effective method of birth control from the time this form is signed until at least 3 months after the last treatment. If you are already using a method of birth control, you would have to check with the study doctor or a member of the study staff to make sure it is acceptable.

If you became pregnant after joining this study, you would have to notify the study doctor immediately. Participation in this study would end, and you would receive counseling and follow-up throughout the pregnancy and for about 6 months after the child is born.

The effects of STEMVAC vaccine or the GM-CSF with your maintenance therapy on fathering a child are also unknown. Men who join this study must also agree to use one or more forms of effective and acceptable birth control from the time this form is signed until at least 3 months after the last treatment.

Non-Physical Risks

If you join this study, non-physical risks are:

- You might not be able to work.

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What are the benefits?

We do not know if this study will help you. You might get better if you receive this treatment but your condition could stay the same or even get worse. We hope the information from this study will help other people with cancer in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say “yes” or “no”. Your regular medical care would not change if you decide to say “no”.

You have other choices for treatment. Each of these choices has risks and benefits. You should talk to your doctor.

Other choices include:

- Standard treatment
- Another research study
- No treatment
- Comfort care

Enrollment in this study may exclude you from other research studies.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form.

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutch/University of Washington Cancer Consortium IRB. An IRB is an independent group of experts that review the study to protect the rights and welfare of research participants.
- Department of Defense and their agents
- The Human Research Protection Office (HRPO) from the Department of Defense (DoD).
- Fred Hutch, , and University of Washington.
- Food and Drug Administration (FDA), Office of Research Protections and other regulatory agencies as required.

We will do our best to keep personal information confidential but we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests, or a court may order study information to be disclosed. Such cases are rare.

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We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

How is my genetic information protected?

A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect genetic information about people who join research studies.

GINA restricts access to genetic information so that it cannot be used for health insurance coverage decisions. GINA prevents health insurance companies or group health plans from:

- Asking for genetic information obtained in research studies, or
- Using genetic information when making decisions regarding your eligibility or premiums.

GINA *does not* help or protect against genetic discrimination by companies that sell life, disability or long-term care insurance.

Would we pay you if you join 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?

You or your insurance company will be billed in the usual manner for tests or procedures that are considered routine and required for the management of your cancer. Routine care is care you would receive whether or not you are in this study. These tests and procedures are billable to you and/or your insurance company. Some examples of routine care include routine maintenance therapy, laboratory blood tests, x-rays, imaging scans (CT or MRI), physician charges and usual medical care.

Ask your study doctor about what procedures are routine care. You may want to talk with your insurance company about its payment policy for routine care given during a research study. If your insurance company does not pay, you may be billed for those charges. Your insurance company may disagree with your study doctor about which tests and/or procedures are considered routine care. If your insurance company believes these tests and/or procedures are related to the research study they may deny payment, which would make you responsible for any charges that are not paid for by the study sponsor. There is never any guarantee with any hospital service that you will not have to pay for any of these services.

The cost of:

- STEMVAC Vaccine mixed with GM-CSF or
- GM-CSF dose alone

Will be provided free of charge for use in this research study.

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You might have unexpected expenses from being in this study. Ask your study doctor to discuss the costs that will or will not be covered. This discussion should include who will pay the costs of treating complications or possible side effects.

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 you believe related to the treatment, contact Dr. Santana (phone number at the end of this consent). Her team 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 specimen leftover. We invite you to donate any leftover specimens for future research to the repository that the Cancer Vaccine Institute (CVI) maintains. You will be asked to sign a separate consent form for this purpose.

If you join this study, you would not have to donate specimens or information for future research. You would be free to say “yes” or “no.” Regular medical care would not change if you say “no.”

If you say “no,” your specimens and information (even if made anonymous) will not be used in future research.

If you donate specimens and information, it would be stored in a secure location. If we want to use your specimens for other research or share it with other scientists for research, an ethics review committee (IRB) would review the request. The IRB would decide if we need to ask you for permission to do the research.

Your donated specimens and information would be used only for research. This research could be done by for-profit companies. Researchers would not report their results to you or your doctors. The research results would not be included in medical records. The results would not affect your medical care.

Research with specimens and information might help develop new products. If these products make money, there is no plan to share the money with the participants who donate the specimens.

If you donate specimens and information for research, you could withdraw the donation at any time by calling Dr. Mary L. Disis, MD at 1-206-616-1823. You would have no penalty for withdrawing the donation, and regular medical care would not change. We could not return donated specimens to you or your doctor, but we might be able to destroy the donated specimens.

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We could not destroy specimens if it is stored or shared without any label saying who donated it. In this case, it could still be used for research.

Your rights

- You do not have to join this study. You are free to say “yes” or “no”.
- 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 this study, we might learn new information that you would need to know. For example, if we learn new information:
    - That may affect your health or well-being.
    - That might make you change your mind about being in this study.

  If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). There is no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.
- Your regular medical care would not change if you join this study.
- If you decide to drop out/withdrawal from the study procedures, we would want you to tell the study doctor You and the study doctor could talk about the follow up care and testing that would help the most.
    - We would want you to come back for the safety/end of treatment visit
    - We would also like to continue to follow your progress and any side affects you may have developed.

A description of this clinical trial will be available on *https://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.

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

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For more information

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

If you have questions about:	**Call:**
This study (including complaints and requests for information)	Kris Kauno, Research Coordinator (206) 616-9538
If you get sick or hurt in this study	Dr. Rafael Santana-Davila or in an emergency or Hematology-Oncology Fellow on-call at 206-598-6100 (24-hour number)
Your rights as a research participant	(206) 667-5900 or email: irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutch Cancer Research Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	(206) 598-1950

Emergency number (24 hours): Dr. Rafael Santana-Davila or Hematology-Oncology Fellow on-call 206-598-6100 (24-hour number)

Do you allow study staff to contact you and/or your doctor regularly for study-related follow-up as described above under “Long-Term Follow-Up? **(Circle one)**

YES **NO** **Initials:** **Date:**

Is it OK if someone contacts you in the future regarding this or other Cancer Vaccine Institute research?

(Circle one)

YES **NO** **Initials:** **Date:**

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Signatures
If you have read this form (or had it read to you), asked any questions, and agree to participate, please sign:

_____ _____:_____ (AM / PM)

Participant's Printed Name Time

_____ _____/_____/_____

Participant's Signature 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.

_____ _____:_____ (AM / PM)

Researcher's Printed Name Time

_____ _____/_____/_____

Researcher's Signature Date

If you served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

_____ _____:_____ (AM / PM)

Witness or Interpreter Printed Name: Time

_____ _____/_____/_____

Witness or Interpreter Signature Date

Protocol: FH10726/P151

Current consent version date: 11/13/2023

Previous consent version date: 07/21/2023

Copies to: Patient

Fred Hutch IRB
Approved
2/7/2024

SCHEDULE OF EVENTS

Visit Time Point	Procedures
Baseline evaluation visit Some procedures may be done up to 60 days prior to the first treatment visit	• Informed Consent • Tumor Imaging (if applicable) and read by RECIST • Medical history and complete physical examination • Vitals signs-including weight • Clinical labs[a, b] • Urine pregnancy test (if applicable) • CT or Ultrasound guided core needle biopsy of tumor (archived tissue may be used at the discretion of the Clinical PIs)
TREATMENT 1 [c] 14 days (+ 3) post pemetrexed/pembrolizumab infusion	• Complete physical examination[d] may use baseline evaluation visit results prior to treatment 1. • Vitals signs-including weight • Urine pregnancy test (if applicable) • Clinical labs[b] • ANA, C3, anti-dsDNA, thyroid function test • Research blood: approximately one cup • Tetanus diphtheria (Td) vaccine • Treatment1 (*STEMVAC vaccine + GM-CSF or GM-CSF alone*) • After treatment monitoring for allergic reaction for a minimum of one hour
Maintenance therapy Approx. 7 days after vaccine 1	• Pembrolizumab with or without pemetrexed
TREATMENT 2 [c] 14 days (+ 3) post pemetrexed/pembrolizumab infusion	• Complete physical examination ✓ Vitals signs-including weight ✓ Assess for any side effects • Urine pregnancy test (if applicable) • Clinical labs[b] • ANA, C3, anti-dsDNA, thyroid function test • Treatment 2 (*STEMVAC vaccine +GM-CSF or GM-CSF alone*) • After treatment monitoring for allergic reaction for a minimum of one hour
Maintenance therapy Approx. 7 days after vaccine 2	• Pembrolizumab with or without Pemetrexed

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Visit Time Point	Procedures
TREATMENT 3 [c] 14 days (+ 3) post pemetrexed/pembrolizumab infusion	• Complete physical examination ✓ Vitals signs-including weight ✓ Assess for any side effects • Urine pregnancy test (if applicable) • Clinical labs[b] • ANA, C3, anti-dsDNA, thyroid function test • Treatment 3 (*STEMVAC vaccine +GM-CSF or GM-CSF alone*) • After treatment monitoring for allergic reaction for a minimum of one hour
Maintenance therapy Approx. 7 days after vaccine 3	• Pembrolizumab with or without Pemetrexed
EVALUATION 1 – At least 3 weeks after THIRD treatment	• Complete physical examination ✓ Vitals signs-including weight ✓ Assess for any side effects • Clinical labs[b] • ANA, C3, anti-dsDNA, thyroid function test • Research blood: approximately one cup • Imaging – CT scan per standard of care and read by RECIST • CT or Ultrasound guided core biopsy of tumor
BOOSTER TREATMENTEVALUATION 2 - At least 9 weeks after THIRD treatment	• Complete physical examination ✓ Vitals signs-including weight ✓ Assess for any side effects • Urine pregnancy test (if applicable and receiving booster vaccine) • Clinical labs[b] • ANA, C3, anti-dsDNA, thyroid function test • Research blood: approximately one cup • For those on study treatment: ○ Booster treatment (*STEMVAC vaccine + GM-CSF or GM-CSF alone*) ○ After treatment monitoring for allergic reaction for a minimum of one hour
POST BOOSTER EVALUATION- At least 3 weeks after BOOSTER treatment	• Complete physical examination ✓ Vitals signs-including weight ✓ Assess for any side effects • Clinical labs[b] • ANA, C3, anti-dsDNA, thyroid function test • Research blood: approximately one cup
LONG TERM FOLLOW-UP	• Twice yearly for 5 years after last visit • Request records from the patient's oncologist[e]

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Visit Time Point	Procedures
[a]Can use standard of care laboratory evaluations if performed 60 days prior to prior to the vaccine visit [b]CBC with differential: white blood cells, red blood cells, platelets; CMP: sugar (glucose) level, electrolyte and fluid balance, kidney function, liver function [c]Treatment administered Day 14 (+ 3 days) after Pembrolizumab with or without pemetrexed infusion [d]May use physical exam that was done prior to treatment 1 [e]Records may include: most recent laboratory evaluation, patients disease status, and recent clinical notes with medical history/physical exam(s)	