Official Title	A Phase II Study of Anti-PD-1 (pembrolizumab) in Combination with Carboplatin to Prevent Progression after Serologic Detection of Recurrent Ovarian Cancer
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UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE
DIVISION OF ONCOLOGY
CANCER VACCINE INSTITUTE (CVI)
Fred Hutchinson Cancer Center

Consent to take part in a research study:

A Phase II Study of Anti-PD-1 (pembrolizumab) in Combination with Carboplatin to Prevent Progression after Serologic Detection of Recurrent Ovarian Cancer

Combination pembrolizumab plus platinum chemotherapy in patients with serologic recurrence of ovarian cancer

PRINCIPAL INVESTIGATOR:
John B. Liao, MD, PhD, University of Washington, (206) 797-2297

EMERGENCY NUMBER (24 hours):
John B. Liao, MD, PhD, University of Washington, Pager (206) 797-2297

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 the clinical response rate of your disease when using a platinum-based chemotherapy (carboplatin) along with pembrolizumab (Keytruda) a medicine that works with your immune system.

If you agree to join the study, you will have an infusion of pembrolizumab on Day 1 of each 6 week cycle, and a one-time infusion of carboplatin two days prior to your first dose of pembrolizumab. Physician exams, blood draws, and review of any side effects will take place on Day 1 of each cycle. You may also have additional blood draws and receive medications if indicated, to prevent some side effects prior to each treatment.

We do not know if pembrolizumab used along with one dose of carboplatin will help treat your cancer/prevent a recurrence and it may cause side effects such as nausea, vomiting, diarrhea, and fatigue, as described later in this form.

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 ovarian, fallopian tube, and primary peritoneal cancer. Up to 26 people (including 4 replacements if needed) will join this study.

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 pembrolizumab along with (one time) carboplatin will fight your cancer. You have previously been treated with carboplatin or cisplatin but your CA-125 is now rising. We want to see if giving pembrolizumab along with carboplatin will work better on killing your cancer cells than your previous carboplatin or cisplatin treatment.

We are studying pembrolizumab (Keytruda). This is medicine that works with your immune system. It is approved for several different cancer but is experimental in your type of cancer.

In this study, we want to learn what effects, good or bad, pembrolizumab has on people with ovarian, fallopian tube, and primary peritoneal cancer. If you join this study, we would give you pembrolizumab and watch carefully for any side effects.

What research tests, procedures, and treatments are done in this study?
If you join this study, we would do these tests and procedures:

Screening phase – some screening procedures may be done prior to the first treatment cycle or happen at the same day as cycle 1.

- 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 30 days of first dose of study drug we may have to perform the scans
- Review your medical history and ensure you meet the eligibility criteria.
- Physical exam with includes vital signs and weight.
- Medication review.

- 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)
    - Blood clotting tests
- We will ensure you have archived tumor available and collect it sometime during the study period for immune testing

Two days prior to your first pembrolizumab you will be given carboplatin (*labs, chemotherapy and related care may be ordered by your physician per standard of care*):

- Clinical blood draw per standard of care
- Carboplatin AUC 6 will be administered as 30-minute IV infusion per standard of care
    - Dose is based on your weight, age and certain lab values
- You may be given medication to help prevent nausea and vomiting per standard of care
- This will be performed most likely at your physician's office
- We will collect information from this visit

Day 1 of each 6 week cycle (up to 24 months or recurrence, whichever comes first)

- Clinical blood draw
    - CBC and CMP
    - Blood clotting tests (every 3 cycles from cycle 1)
    - ANA, T3, FT4, TSH (autoimmune and thyroid tests) (every 3 cycles from cycle 1)
    - CA-125 (if not done 2 days prior)
- Research blood draw
    - Approximately one cup of blood will be collected for research testing so we can measure your immunity (immediately prior to cycles 1, 3, and 6 and after that it will be performed for every 6 cycles)
- Physical exam which includes vital signs and weight
- Medication review
- Side effect(s) review
- Pembrolizumab 400mg will be given as a 30 minute IV infusion

  - You may be given premedication prior to this infusion on discretion of the study doctor

- Tumor imaging* (prior to cycles 3, and 5 then approximately every 3 months)

  *May be ordered by your physician per standard of care

End of treatment/discontinuation visit/Safety Visit

Approximately 30 days after your last dose of pembrolizumab or before you start another type of cancer treatment, we will ask you to come back to the research clinic for a follow-up visit. We would like to do the following:

- Clinical blood draw
  - CBC w/ differential
  - CMP
  - CA-125
  - Blood clotting tests
  - Autoimmune testing
- Physical exam which includes vital signs and weight
- Medication review
- Side effects review
- Re-Treatment Period Only – Research Blood Draw

Long-term Follow-up

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 pembrolizumab in combination with carboplatin.

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.

Re-Treatment Period

If you have stopped the initial study treatment or a re-treatment period of study treatment (after at least 1 pembrolizumab) you may be eligible for up to an additional 9 cycles of the pembrolizumab treatment (approximately 1 year).

If you are eligible to participate in the re-treatment period you will follow the same procedures as listed above. That includes receiving another dose of carboplatin prior to starting the pembrolizumab again.

You will continue to follow the same procedures as listed above.

How long would you stay in this study?
If you join this study, you could have treatment with pembrolizumab for up to 2 years unless your cancer gets worse or you have side effects that are not acceptable. Each treatment cycle is 6 weeks.

If you stopped pembrolizumab after achieving a complete remission, you may be eligible for re-treatment for up to a year if your cancer progresses after you were off study. We will follow similar procedures as listed above under "What research tests, procedures, and treatments are done in this study?"

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.
- 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.

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.

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 pembrolizumab and carboplatin could cause side effects we do not know about yet. We carefully watch everyone in the study for side effects.

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* drugs. Side effects that are common to both drugs appear in **bold**. Their incidence may increase when the drugs are used *together.*

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 taking pembrolizumab and carboplatin. In some cases, side effects can last a long time or never go away.

Pembrolizumab

Pembrolizumab, given alone, works by helping your immune system to fight your cancer. However, pembrolizumab can cause your immune system to attack normal organs and tissues in your body and can affect the way they work, which can result in side effects. These side effects may be serious (i.e. causing hospitalization or be life threatening), may result in death, and/or may occur after you stop taking pembrolizumab.

Likely (≥10% of patients)	Less likely (≥5%)	Rare but serious (≥0.2%)
Anemia	**Fatigue**	Pneumonitis*
Fatigue	Decreased appetite	**Nausea**
Itching	Hypothyroidism	**Diarrhea**
Cough	Thyroiditis	Colitis
Nausea	Itching	Fever
Weakness	**Diarrhea**	Pneumonia
Diarrhea	Arthralgia	Encephalitis
Decreased appetite	Weakness	Hyperthyroidism
Shortness of breath	**Nausea**	Hypoparathyroidism
Arthralgia	Myalgia	Arthritis
Rash	Vitiligo	Sarcoidosis
Constipation		Autoimmune hepatitis
Back pain		**Shortness of breath**
Swelling (limbs)		Myasthenic syndrome
Rash		Vasculitis - Inflammation of the blood vessels (Symptoms will depend on the particular blood vessels that are involved in the inflammatory process, for example; if it is your skin, you may get a rash. If your nerves are not getting enough blood, you could have numbness and weakness. You may also experience fever, weight loss, and fatigue)
Headache		Sclerosing cholangitis
Vomiting		Low sodium in blood
Fever		Adrenal insufficiency
		Immune-mediated myocarditis
		Sevens-Johnson Syndrome (SJS)

Likely (≥10% of patients)	Less likely (≥5%)	Rare but serious (≥0.2%)
		Toxic Epidermal Necrolysis (TEN) Graft vs. host disease (GVHD) in patients with a history of hematopoietic stem cell transplant (HSCT). This condition can lead to death If you have had a solid organ transplant, you may experience rejection of the transplanted organ Inflammation or swelling of the nerve fibers of the eye which send visual information from your eye to your brain. This health condition often has a sudden onset of vision loss, loss of color vision, pain when moving your eyes, and/or loss of peripheral vision. It may affect one or both eyes at the same time (optic neuritis). Inflammation of the stomach (gastritis). You may have pain in your belly, feel full, or sick to your stomach. You may also experience nausea, vomiting or loss of appetite. Low number of red blood cells (cells that carry oxygen) due to destruction of red blood cells (hemolytic anemia). You may feel weak, tired, lightheaded, short of breath, or have a fast heartbeat. You may also experience difficulty with physical exercise, pale or yellow skin, dark urine, or fever. Not enough pancreatic enzymes (proteins that break down food) that leads to poor digestion of food (exocrine pancreatic insufficiency). You may have bloating, gas, discomfort in your belly, diarrhea, abnormal stool that is oily, or weight loss. Inflammation of the protective sac surrounding your heart (pericarditis) which can cause sharp chest pain and shortness of breath (especially when lying flat), fever, and a fast or irregular heartbeat. In severe cases, your heart may have difficulty pumping blood throughout your body.

* If you have a history of pneumonitis that required steroids or currently have pneumonitis, you will not be able to enroll in the study.

Carboplatin

Although you will only be getting one dose of carboplatin on this study, below are possible side effects.

Likely (>20% of patients)	Less likely (4-20%)	Rare but serious (<3%)
• Hair loss • Vomiting, nausea • Infection, especially when white blood cell count is low • Anemia which may cause tiredness, or may require blood transfusions • Bruising, bleeding • Belly pain	• Diarrhea, Constipation • Numbness and tingling in fingers and toes • Allergic reaction: which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Changes in taste • Changes in vision	• Damage to organs which may cause hearing and balance problems

Risk of CT Scan (if not covered by 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 chest 7 mSv
- CT abdomen 8 mSv
- CT pelvis 6 mSv

Reproductive Risks

Chemotherapy could cause sterility (unable to have children).

Taking the combination of pembrolizumab and carboplatin may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant. Therefore, you cannot 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 four months after the last dose of pembrolizumab. 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 become 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.

Risks of Blood Tests

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

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

- You might not be able to work.
- Results of genetic testing might be released by accident. This risk is very low, because we keep personal information private. If these results became known, you could have problems with family members or insurance.

What are the benefits?
We do not know if this study will help you. We are testing the combination of pembrolizumab and carboplatin to see its effects on people with ovarian, fallopian tube, and primary peritoneal cancer. 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 of 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.
- Department of Defense and their agents
- Merck & Co., Inc. and their agents. Merck if providing pembrolizumab (study drug) free of charge.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Center 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.

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

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

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 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.

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.

Pembrolizumab is being provided by Merck & Co., Inc. free of charge for use in this study.

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 **Dr. John B. Liao**. 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 specimen leftover. We would like you to donate any leftover specimens for future research to the repository that the Cancer Vaccine Institute (CVI) has. This future research may relate to immune response tests, or separate consent form for this purpose.

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).

- Your regular medical care would not change if you join this study. 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.
- If you decide to drop out/withdrawal from the study procedures, we would want you to tell the study doctor so they tell you about the effects of stopping the pembrolizumab and carboplatin. 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 effects 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
- Take study medications as directed
- Prevent pregnancy
- Tell us about side effects

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)	Kellie Burton, BSN, RN (206) 616-9538
If you get sick or hurt in this study	(206) 797-2297 Dr. John Liao (Principal Investigator)
Your rights as a research participant	(206) 667-5900 or email: irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	(206) 598-1950

Emergency number (24 hours): (206) 797-2297

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 study staff contacts you in the future regarding this or other Cancer Vaccine Institute (CVI) research?

(Circle one)

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

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: FH10312/P150

Current consent version date: 11.14.2024

Previous consent version date: 04.15.2024

Copies to: Patient

SCHEDULE OF EVENTS

Visit time point	Procedures
Screening	• Informed Consent Conference • Ensure there is archival tissue available to be collected sometime during study • Full physical examination • Medical History review • Medication Review • Vital signs and weight • Tumor Imaging[a] - if not done 30 days prior to Cycle 1 • Labs[b]: Blood clotting, CBC w/ differential, Comprehensive Serum Chemistry Panel (CMP)
Two days prior to cycle 1 treatment	• Carboplatin administration[c]
Cycle[f] 1	• Full physical examination • Review adverse events • Concomitant Medication Review • Vital signs and weight • Labs[b]:CBC, CMP, autoimmune and thyroid tests, CA-125 • Research blood draw[d] • Pembrolizumab administration (± 3 days)
Cycle[f] 2	• Full physical examination • Review adverse events • Concomitant Medication Review • Vital signs and weight • Labs[b]: CBC, CA-125, CMP • Pembrolizumab administration (± 3 days)
Cycle[f] 3	• Tumor Imaging[a] - prior to infusion visit +/- 7 days • Full physical examination • Review adverse events • Concomitant Medication Review • Vital signs and weight • Labs[b]: CBC, CMP, autoimmune and thyroid tests, blood clotting tests, CA-125 • Research blood draw[d] • Pembrolizumab administration (± 3 days)
Cycle[f] 4	• Full physical examination • Review adverse events • Concomitant Medication Review • Vital signs and weight • Labs[b]: CBC, CA-125, CMP • Pembrolizumab administration (± 3 days)
Cycle[f] 5	• Tumor Imaging[a] - prior to infusion visit +/- 7 days • Full physical examination • Review adverse events • Concomitant Medication Review • Vital signs and weight • Labs[b]: CBC, CA-125, CMP • Pembrolizumab administration (± 3 days)
Cycle[f] 6	• Full physical examination • Review adverse events

Visit time point	Procedures
	• Concomitant Medication Review • Vital signs and weight • Labs[b]: CBC, CMP, autoimmune and thyroid tests, blood clotting test, CA-125 • Research blood draw[d] • Pembrolizumab administration (± 3 days)
Cycle[f] 7[f]	• Tumor Imaging[a] - prior to infusion visit +/- 7 days • Full physical examination • Review adverse events • Concomitant Medication Review • Vital signs and weight • Labs[b]: CBC, CA-125, CMP • Pembrolizumab administration (± 3 days)
Cycle[f] 8[e]	• Review adverse events • Concomitant Medication Review • Full physical examination • Vital signs and weight • Labs[b]: CBC, CA-125, CMP • Pembrolizumab administration (± 3 days)
End of treatment/discontinuation visit (Safety Follow up) approximately 30 days post treatment or before the initiation of a new anti-cancer treatment	• Review adverse events • Concomitant medication review • Full physical examination • Vital signs and weight • Labs[b]: CBC, CA-125, CMP • Re-Treatment Period Only – Research Blood Draw[g]
Every six months	• Tumor Imaging[a] • Collect records from oncologist

[a] CT or MRI/CT per standard of care.

[b] CBC with differential: Complete Blood Count; CMP: Complete Metabolic Panel: Blood clotting labs: ANA, T3, FT4, TSH: autoimmune and thyroid tests: CA-125: tumor marker; urinalysis only as needed

[c] One dose of carboplatin per standard of care. This will be performed most likely at your physician's office

[d] Approximately one cup of blood for immune evaluation. Please hydrate well prior to this visit. After cycle 6, this will occur every 6 cycles[e] After cycle 8, repeat cycles 6,7,8 until off treatment

[f] Cycles are every 6 weeks plus or minus 3 days

[g] Re-treatment phase only: Research blood draw may be collected at End of Treatment Visit or 30 Day Safety Follow-up Visit.