IRO received 11/23/21

UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE
DIVISION OF ONCOLOGY
TUMOR VACCINE GROUP (TVG)

Consent to take part in a research study:

Anti-PD-1 Therapy in Combination with Platinum Chemotherapy for Platinum Resistant Ovarian, Fallopian Tube, and Primary Peritoneal Cancer

PRINCIPAL INVESTIGATOR: **John B. Liao, MD, PhD**

EMERGENCY NUMBER: 206-797-2297 (pager)

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 a 21 day cycle, and carboplatin on Days 8 and 15. 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 to prevent some side effects prior to each treatment.

We do not know if pembrolizumab used along with carboplatin will help treat your cancer and it may cause side effects.

You do not have to join this study. You could choose to receive standard methods to treat your cancer. 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.

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 27 people will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific 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 carboplatin will fight your cancer. You have previously been treated with carboplatin or cisplatin but your cancer came back within 6 months of your treatment. 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. This is medicine that works with your immune system. It is approved for several different cancers 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 – Screening procedures may be done up to 28 days prior to Day 1 of 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 28 days of first treatment
- Review your medical history and ensure you meet the eligibility criteria.
- Physical exam which includes vital signs, and weight.
- Clinical blood draw:
    - Routine blood tests to evaluate kidney, liver, and blood system function (CBC w/differential and Comprehensive Serum Chemistry Panel)
    - Blood clotting tests (PT/INR and aPTT)
- Urinalysis
- We will ensure you have archived tumor available

Day 1 of each 21 day cycle

- Clinical blood draw
    - Routine blood tests to evaluate kidney, liver, and blood system function
    - PT/INR and aPTT (every 3 cycles from screening/cycle 1)
    - ANA, T3, FT4, TSH (every 3 cycles from cycle 1)
    - CA 125
- 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, 4, and 6 after that it will be performed every 6 cycles)
- Physical exam which includes vital signs and weight.
- Medication review
- Side effect(s) review
- Pembrolizumab 200 mg will be given as a 30 minute IV infusion
- Tumor Imaging* (prior to cycles 4, and 8 then approximately every 3 months

  *Will be ordered by your physician per standard of care

Days 8 and 15 of each cycle – these procedures will be performed at your physician's office. We will collect the information from these visits.

- Clinical blood draw per standard of care
- Carboplatin AUC 2 will be administered as a 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

How long would you stay in this study?

If you join this study, you could have treatment with pembrolizumab and carboplatin for up to 2 years unless your cancer gets worse or you have side

effects that are not acceptable. If you have bad side effects due to the carboplatin, you may be able to stop that drug and continue the study with pembrolizumab alone.

If you stopped pembrolizumab and carboplatin after achieving a complete remission you may be eligible for re-treatment for up to a year if your cancer progresses.

End of treatment/Discontiuatiuon visit**

After you stop the pembrolizumab or carboplatin in this study, we will ask you to come back to the research clinic for a follow-up visit. Wwe would like to do the following:

- Clinical blood draw
    - Complete blood count
    - Comprehensive chemistry panel
    - CA 125
    - PT/INR and aPTT
    - ANA, T3, FT4, TSH
- Physical exam which includes vital signs and weight
- Medication review
- Side effects review

Safety follow-up visit**

- 30 days after your last dose of pembrolizumab or carboplatin or before you start another type of cancer treatment, we will collect records from your oncologist to see how you are doing. We will continue to follow any side effects you may have (except mild ones) until they disappear, become mild or back to what you reported at your first visit

**The Disconiutation Visit and Safety Follow Up visit may be the same visit.

Long Term Follow-up

Long term follow-up means keeping track of someone's medical condition for a long time. If you join this study but have to stop the trial for a reason other than disease progression we will move you into the follow-up phase of the trial.

- Imaging apporximately every 12 weeks per standard of care for the first year and every 6 months for year 2.

- We will keep in touch with you or your physician to see how you are doing every three months until you withdraw your consent or the study ends-whichever occurs first.

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

- Confirmed radiographic disease progression.
- If your physician feels that it is in your best interest to go off study.
- Unacceptable side effects.
- Another illness that prevents further infusions.
- You become pregnant.
- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The 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*. Other side effects could occur when we use these drugs *together*.

Side effects may be mild or very serious and possibly result in death. 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
Overall, as of 03-MAR-2018, approximately 25,519 patients have been treated with pembrolizumab in clinical studies.

Pembrolizumab, given alone, works by helping your immune system to fight your cancer. However, pembrolizumab can also 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 (0.2-10%)	Rare but serious (<0.2%)
• **Anemia** • **Fatigue** • Itching • Cough • **Nausea** • **Diarrhea** • Arthralgia • Rash • **Constipation** • Headache • **Vomiting** • Back pain • Swelling (limbs)	• Decreased appetite • Hypothyroidism • Thyroiditis • Weakness • Myalgia • **Vitiligo**	• Pneumonitis* • **Severe diarrhea** • Colitis • Fever • Autoimmune hepatitis • Hyper-thyroidism • **Shortness of breath** • **Severe nausea** • Low sodium in blood • Adrenal insufficiency • Pneumonia • Immune-mediated myocarditis • Stevens-Johnson Syndrome (SJS) • Toxic Epidermal Necrolysis (TEN) • Encephalitis • Scarcoidosis • Myasthenic syndrome • Graft vs. host disease (GVHD) in patients with a history of allogenic hematopoietic stem cell transplant (HSCT). Sometimes this condition can lead

Likely (≥10% of patients)	Less likely (0.2-10%)	Rare but serious (<0.2%)
		to death. • If you have had a solid organ transplant, you may experience rejection of the transplanted organ. • Arthritis (inflammation of the joints which may include joint pain, stiffness and/or swelling)

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

Carboplatin

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 **(fatigue)**, 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

Risks of Blood Tests

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

Radiation Exposure
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 likely zero.

- CT scan of the head: 2 mSv
- 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 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 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 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.

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

- You might not be able to work.

- Results of genetic tests 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 the combination of pembrolizumab and carboplatin will help treat your cancer. We hope the information we learn will help people with your type of cancer in the future.

We do not know if this study would 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 or healthcare provider about these choices.

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, 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.

- Merck & Co., Inc. and their agents. Merck is providing pembrolizumab (study drug) free of charge as well as financial support for the study.

- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.

- Fred Hutchinson Cancer Research Center, University of Washington, and Seattle Cancer Care Alliance.

- Food and Drug Administration (FDA).

- 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 participation would be made part of your permanent medical record. This information would 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.

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 prevent 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?
There are no extra costs for being in this study. 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 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 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

- 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 the 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 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 could 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 End of Treatment and Safety Follow-Up visits.
    - 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 **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.

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

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

For more information
If you have questions or concerns about this study, you could 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)	Doreen Higgins, BSN, RN, OCN 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	206-667-4867 (Karen Hansen, Director of Institutional Review Office, Fred Hutchinson Cancer Research Center) 206-543-0098 (Human Subjects Division, University of Washington)

Emergency number (24 hours): 206-797-2297Signatures
If you have read this form (or had it read to you), asked any questions, and agree to participate, please sign:

Participant / Printed Name, Signature, and Time/Date

Is it OK if someone 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.

Person obtaining consent signature / Printed Name, Signature, Time/Date

Protocol: IR# 9740/ TVG 141
Current version date: 08/20/2018
Previous version date: 04/05/2018
Copies to: Research Chart, Research Patient, Clinical Research Center

SCHEDULE OF EVENTS

Visit Time Point	Procedures
Screening Phase Screening procedures may be done up to 28 days prior to Day 1 of first treatment cycle or at the same time	• Informed Consent • Review medical history and eligibility review • Physical exam ○ Vitals signs-including, height, weight • Clinical labs[a] • Urinalysis • Tumor imaging – CT or MRI/CT[c] if not completed within 28 days of first treatment • We will ensure you have archived tumor available
Treatment Cycles are 21 Day Cycles	*Patients may receive up to 24 cycles of treatment*

Day 1	• Clinical labs[a]
	• Research blood[b]
	  ○ Prior to cycle 1, 4 6; then collected every 6 cycles
	• Physical exam
	  ○ Vitals signs-including, height, weight
	• Medication review
	• Side effect(s) review
	• Administration of pembrolizumab 200 mg given as a 30 minute IV infusion
	• Tumor imaging – CT or MRI/CT[c]
	  ○ Prior to cycle 4 and 8, then approximately every 3 months
	  ○ To be done by your own oncologist per standard of care

Days 8 and 15 These procedures will be performed at your physician's office.	We will collect the following information from your physician: • Clinical labs • Other related documents

End of Treatment/Discontinuation	• Complete physical examination
	  ○ Vitals signs-including weight
	  ○ Assess for any side effects
	• Side effect(s) review

Safety Follow-Up Visit(s) These procedures will be performed at your physician's office.	• Side effect(s) review (if applicable)
Long-Term Follow-Up Visits[d]	• Tumor imaging – CT or MRI/CT[c] ○ Every 12 weeks (per standard of care) • We will continue to keep in touch with you or our physician to see how you are doing every three months

[a] CBC w/differential and comprehensive serum chemistry panel (CMP); PT/INR and aPTT (screening phase then every 3 cycles); ANA, T3, FT4 and TSH (prior to cycle 1 then every 4 cycles); CA125 (starting prior to cycle 1))

[b] Please drink plenty of fluids prior to visits requiring large volume blood draws

[c] Performed per standard of care

[d] This will continue until you withdraw consent or the study ends – whichever comes first