IRO received 12/22/20

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

Consent to take part in a research study:

A Phase II Study of Concurrent IGFBP-2 Vaccination and Neoadjuvant Chemotherapy to Increase the Rate of Pathologic Complete Response at the Time of Cytoreductive Surgery

PRINCIPAL INVESTIGATOR: **John B. Liao, MD, PhD, University of Washington**

EMERGENCY NUMBER: 206-797-2297 (pager), John B. Liao, M.D., PhD

Your doctors are inviting you to participate in a research study. The purpose of this research is to determine if adding a cancer specific vaccine (IGFBP-2 plasmid based vaccine), that works with your immune system, to your standard neoadjuvant chemotherapy (carboplatin/paclitaxel/) will help the chemotherapy fight your cancer better.

If you agree to join the study, you will begin receiving chemotherapy with your own oncologist. Approximately two weeks after each chemotherapy you will receive a cancer vaccine under your skin in your arm or leg for up to 3 vaccines. Before each vaccine you will have a physical exam, blood draw, and review of any side effects from the vaccine. We do not know if adding this vaccine with your chemotherapy 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 without the addition of the IGFBP-2 vaccine. In this consent 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.

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 will 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 just been diagnosed with ovarian cancer and have not received chemotherapy or surgery yet. Up to 38 people may 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 the vaccine along with your chemotherapy enhances the effectiveness of the chemotherapy. The vaccine targets IGFBP-2. IGFBP-2 is a protein found in the blood and tumor cells of most women who have been diagnosed with ovarian cancer. Too much IGFBP-2 has been associated with more invasive disease. One possible way to get rid of IGFBP-2 on tumor cells is simply to encourage your own immune system to generate an immune response against the tumor cells expressing IGFBP-2. Immunizing you with a vaccine against IGFBP-2 may do this.

The vaccine is made up of DNA which is a natural substance in every living organism that helps make the proteins that cause cells in your body to function. The DNA we use is isolated from a bacteria and a portion of the IGFBP-2 protein code (DNA) is inserted. The IGFBP-2 vaccine has previously been tested as a vaccine alone.

The vaccine used in this study is not approved by the Food and Drug Administration (FDA) for commercial use; however, the FDA has permitted its use in this research study.

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

<u>Initial visit (prior to the start of your chemotherapy)</u>

- Informed consent conference. Review consent, have all your questions answered so you can make an informed decision to join the study or not.
- Review your medical history and ensure you meet the eligibility criteria.
- Physical exam which includes vital signs, medication review, and weight.
- Clinical blood draw:
    - Routine blood tests to evaluate kidney, liver, and blood system function
    - ANA, C3, anti-dsDNA to screen for any autoimmune disorders

- Thyroid function tests to monitor for any autoimmunity specific to your thyroid
- CA-125 a tumor marker for ovarian cancer

- Research blood draw
  - Up to one cup of blood will be collected for research testing so we can measure your immunity.

- Archive Tissue Collection
  - If available, we would collect tissue from your primary diagnosis to be able to compare it to your tissue from your surgery after your complete the study treatment.

Vaccinations

Vaccinations will be approximately given two weeks after each chemotherapy visit for a total of 3 vaccine visits. Before each vaccine you will have:

- Physical exam which includes vital signs, weight and a urine pregnancy test (if applicable)
  - If you are pregnant you will not be able to receive the study vaccine..
- Medication review
- Side effect(s) review

You must stay in the clinic for at least one hour after each vaccine to monitor you for any allergic reaction.

Prior to the first vaccine you will have a tetanus vaccination if you haven't had one in the last 6 months. This will help us measure your overall immune response.

After completion of vaccinations

After you have finished the vaccines you will enter the follow up part of the study.

About one to two weeks after your last vaccine and before your surgery:

Physical exam which includes vital signs, and weight.

- Clinical blood draw:

  - Routine blood tests to evaluate kidney, liver, and blood system function
  - ANA, C3, anti-dsDNA
  - Thyroid function tests
  - CA-125

- Research blood draw
  - Up to one cup of blood (depending on your blood counts) will be collected for research testing so we can measure your immunity.

- After your surgery we will collect a piece of your tissue not needed for your clinical care for biomarker research. The tumor tissue sample we collect will only be used for research.

Approximately six months after your last vaccine, you will come back again for the following procedures:

- Physical exam which includes vital signs, and weight.
- Clinical blood draw:
  - Routine blood tests to evaluate kidney, liver, and blood system function
  - ANA, C3, anti-dsDNA
  - Thyroid function tests
  - CA-125
- Research blood draw
  - Up to one cup of blood (depending on your blood counts) will be collected for research testing so we can measure your immunity.

<u>Long-Term Follow-Up</u>

Long-term follow-up means keeping track of someone's medical condition for a long time. If you join this study we would check with your oncologist to see how you are doing by collecting notes, labs, and imaging reports. This would occur once a year for 5 years. This information will help us learn about the long term effects of the IGFBP-2 plasmid based vaccine in combination with carboplatin/paclitaxel.

How long would you stay in this study?
If you join this study, there will be 5 research visits to the University of Washington (UW) Clinical Research Center over a period of approximately 10 weeks for study treatment and an additional follow-up, non-treatment visit, 6 months after your last vaccine.

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

- Unacceptable side effects.
- Another illness that prevents further infusions.
- They think it is in your best interest not to continue in the study.
- You not able or willing to follow study procedures.
- You want to enroll in another treatment trial.
- You become pregnant.
- The whole study is stopped.

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. We may ask you to undergo one final physical exam, which includes weight, vital signs, symptom assessment and blood collection, if applicable.

What are the side effects (risks)?
In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. Although we have given the IGFBP-2 vaccine to 25 women with a history of ovarian cancer and didn't see any serious side effects we have never given this vaccine with chemotherapy. We gave a total of 86 vaccines.

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

Risks of Blood Tests

Likely	Less likely	Rare but serious
Pain	Bruising Light-headedness Fatigue Fainting	Infection

Risks of Tetanus Diphtheria* Immunization

Likely	Less likely	Rare but serious
Redness, pain and swelling at site Mild fever Decreased appetite	Hard lump at the site Allergic reactions such as: hives, rash, and itching Fever > 102°F	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 vaccine may require medication or lead to hospitalization or death Swelling, severe pain, bleeding and/or redness in the arm where the shot was given

*If you have a history of an allergic reaction to the tetanus immunization, we will not give you one and you can still continue to be in the study.

Risks of IGFBP-2 Vaccination(s)

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

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

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

Likely	Less likely	Rare but serious
Local reactions at the site of injection Low grade fever (Less than 100.5° F) Chills Pain in the bones, muscles, chest, abdomen, or joints Nausea	Kidney and liver problems Rashes Liver enlargement Low blood pressure	Fluid retention (including fluid in lungs or around the heart) Blood clotting, including blood clots in the leg veins that can break loose and go to the lung Increased platelets, low albumin (a protein found in your blood), increase of liver enzymes Rapid or irregular heartbeat or

Likely	Less likely	Rare but serious
Vomiting Diarrhea Flu-like symptoms including fatigue, weakness, headache Decreased appetite Increased white blood cell count		other heart problems Allergic reaction, including shortness of breath, dizziness, a feeling of fainting, hives, and difficulty breathing caused by swelling of the mouth, face, tongue or throat Worsening of pre-existing fluid accumulation in arms and legs, in the lungs and around the heart that may result in breathing problems and heart failure Neurologic syndrome called Guillain-Barré syndrome, where a person's own immune system damages their nerve cells, causing muscle weakness and sometimes paralysis Temporary loss of consciousness

Risk of Generation of an Immune Response to Normal Cells

It is unknown whether generating an immune response to this specific protein on your cells will have any effect on normal cells.

- We will be monitoring you closely for signs of immune damage to normal cells. We will be looking for diarrhea, development of any unusual rashes and changes in your liver, kidney, and blood function through blood tests.
- Medicine may be administered if you develop any autoimmune symptoms. A severe autoimmune reaction could cause death.

Likely	Less likely	Rare but serious
None	Skin rashes Diarrhea	A severe autoimmune reaction could cause death

Allergic Reaction Monitoring

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

Side effects may be mild or very serious. Medicines could be given to help lessen side effects. In some cases, side effects can last a long time or never go away. There also is a risk of death.

Chemotherapy
You will be receiving Carboplatin and Paclitaxel from your own oncologist per standard of care. Your oncologist's team can help you deal with these effects should they occur.

Reproductive Risks
- Patients should not become pregnant while in this study
- You should not nurse a baby after enrolling into this study
- For patients who are having sex that could lead to pregnancy, you must agree to use contraception for the duration of the study
    - Check with a study doctor about birth control methods, some common methods might not be appropriate
- There may be long term effects on fetal tissue that we are not aware of

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 a vaccine (IGFBP-2) in combination with chemotherapy will help treat your cancer. We hope the information we learn will help people with ovarian cancer in the future.

We do not know if this study would 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 ovarian 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.
- 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,.
- Food and Drug Administration (FDA).
- Office for Human Research Protections (OHRP).
- 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 would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see the 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?
If you join this study, you or your insurance company would have to pay for the costs of standard treatment 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. His 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.

Future genetic research
Several generic databases are available to help researchers understand different diseases. These databases contain DNA code and medical information from participants who have various diseases.

As part of this study, we would like to release DNA code and information about your medical condition into a genetic database in order to help future research. The genetic database would not contain names, addresses, or other information that could be used to identify you.

The DNA code in a genetic database cannot be used by itself to identify any specific person. A researcher who already has DNA code about you could use information from a genetic database to learn more about you. Once we release information to a genetic database, we no longer have any control over the use of this information.

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 need to know. For example, some information may affect your health or well-being. Other information 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. You would have 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, we would want you to tell the study doctor. The doctor could tell you about the effects of stopping the vaccine. You and the doctor could talk about the follow-up care and testing that would help the most.
    - We would want you to come back for a follow up visit if you leave the study.
    - We would like to continue to follow your progress and any side effects you may have developed because of the vaccine.

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
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): 206-797-2297

Read each question and think about your choice. When you decide on each question, please circle **YES** or **NO**.

Is it OK if we send your genetic information to one or more databases for future research? (circle one) **YES** **NO**

Is it OK if someone from the Tumor Vaccine Group contacts you in the future regarding this or other TVG research? (Circle one)			
YES	**NO**	Initials:	Date:

Signatures

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 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, and Date

Protocol: 9760/144
Current version date: 07/19/2018
Previous version date: 06/28/2017
Copies to: Research Chart, Research Patient, Clinical Research Center

Calendar of Events

Visit Time Point	Procedures
First Visit- prior to the start of your chemotherapy Some procedures may be done up to two weeks prior to initial vaccine visit	• Consent • Medical history and complete physical examination • Vitals signs-including weight • Baseline symptom assessment • Routine blood tests to evaluate kidney, liver, and blood system function (CBC, CMP) • ANA, C3, anti-dsDNA • Thyroid function tests • CA-125 • Research blood: approximately 200 mls* • If available, collect archived tissue from primary diagnosis
First Vaccine: Approx. 2 weeks after chemotherapy	• Medical history and complete physical examination • Vitals signs-including weight • Urine pregnancy test (if applicable) • Baseline symptom assessment (if not previously collected) • Tetanus diphtheria (Td) immunization • IGFBP-2 vaccine • After vaccine monitoring for allergic reaction for a minimum of 60 minutes
Second Vaccine: Approx. 2 weeks after chemotherapy	• Medical history and complete physical examination • Vitals signs-including weight • Urine pregnancy test (if applicable) • Symptom/toxicity assessment • IGFBP-2 vaccine • After vaccine monitoring for allergic reaction for a minimum of 60 minutes
Third Vaccine: Approx. 2 weeks after chemotherapy	• Medical history and complete physical examination • Vitals signs-including weight • Urine pregnancy test (if applicable) • Symptom/toxicity assessment • IGFBP-2 vaccine • After vaccine monitoring for allergic reaction for a minimum of 60 minutes

Visit Time Point	Procedures
Approx. 1 week after final vaccine Prior to surgery	• Medical history and complete physical examination • Vitals signs-including weight • Symptom/toxicity assessment • Routine blood tests to evaluate kidney, liver, and blood system function • ANA, C3, anti-dsDNA • Thyroid function tests • CA-125 • Research blood: approximately 200 mls* • Collect tissue from surgery: After your surgery we will collect a piece of your tissue not needed for your clinical care for biomarker research.
Approx. Month 6 After last vaccine	• Medical history and complete physical examination • Vitals signs-including weight • Symptom/toxicity assessment • Routine blood tests to evaluate kidney, liver, and blood system function • ANA, C3, anti-dsDNA • Thyroid function tests • CA-125 • Research blood: approximately 200 mls*
Long-Term Follow-Up Once yearly follow-up for 5 years	• Collection of physician notes to review toxicity and clinical status
* Please hydrate sufficiently prior to visits due to a large amount of blood being drawn.	