Consent Form

Study Title for Study Participants: Testing the Addition of M6620 (VX-970) to Approved Chemotherapy in Recurrent Platinum Sensitive Ovarian Cancer, **Peritoneal, and Fallopian Tube Cancer**

(Phase 1)

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

9948 / MC1563: Phase 1 Dose Escalation and Expansion Cohort Trial of Carboplatin and Gemcitabine with or without M6620 (VX-970) in First or Second Recurrence Platinum-Sensitive Epithelial Ovarian, Peritoneal, and Fallopian Tube Cancer

What is the usual approach to my platinum sensitive ovarian cancer?

You are being asked to take part in this study because you have ovarian, peritoneal or fallopian tube cancer that has recurred.

Women who are not in a study are usually treated with chemotherapy. There are several FDA approved combination chemotherapy treatments that are commonly used, one of which is carboplatin and gemcitabine. These treatments can reduce symptoms and may stop the tumor from growing for several months or more.

Your doctors have recommended the standard of care carboplatin and gemcitabine to treat your cancer. In some cases, physicians recommend the addition of bevacizumab to carboplatin and gemcitabine. This is also an Food and Drug Administration (FDA) approved treatment. Please discuss with your doctor if you would like more information regarding the advantages and disadvantages of receiving bevacizumab with carboplatin and gemcitabine. If you elect to receive bevacizumab with carboplatin and gemcitabine, you cannot participate in the present study.

Occasionally recurrent platinum sensitive ovarian cancer is treated with additional surgery. The feasibility of this option should be discussed with your doctor.

If your tumor shrinks or is no longer visible on imaging after treatment with the carboplatin and gemcitabine, there is the option to get maintenance treatment with a class of oral medications called poly adenosine diphosphate-ribose polymerase (PARP) inhibitors. This is an option for you whether or not you enroll in this clinical trial. Please discuss with your doctor if you would like more information regarding this option. If you elect to be treated with a PARP inhibitor, that therapy would start after completion of chemotherapy on the present protocol and would not impact your ability to participate in the present study.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to take any of the many usual approaches described above
- you may choose to take part in a different study, if one is available or
- you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms

Why is this study being done?

The purpose of this study is to compare any good and bad effects of using M6620 (VX-970) along with the usual chemotherapy. M6620 (VX-970) is not approved by the FDA and is considered investigational or experimental. M6620 (VX-970) has been tested in humans by itself or in combination with other chemotherapy agents for various diagnoses. The addition of M6620 (VX-970) to the usual chemotherapy could shrink your cancer but it could also cause side effects. The combination of M6620 (VX-970) with carboplatin and gemcitabine is also considered experimental.

There are two parts to this study. The first part of the study is known as the 'phase 1' part and the second part of the study is known as the 'randomized phase 2' part. You are being asked to join the phase 1 part of the study. The phase 1 part of the study tests different doses of M6620 (VX-970) in combination with carboplatin and gemcitabine to establish the recommended phase 2 dose. This will be the first time that the combination of carboplatin, gemcitabine and M6620 (VX-970) is being tried in people.

There will be about 27 people participating in the phase 1 part of the study. About 31 people total will be taking part in this study.

What are the study groups?

In the phase 1 part of the study, all participants will receive the standard of care carboplatin and gemcitabine chemotherapy. The gemcitabine dose may vary from the standard dose. Different doses of the study drug M6620 (VX-970) and gemcitabine will be given to several study participants, including lower doses of the prescribed, approved gemcitabine dose. Treatment in this study will follow a schedule of 21-day long periods and each 21-day period is known as a 'cycle'. M6620 (VX-970) will be given intravenously (IV, through a vein) twice per cycle, on days 2 and 9. Carboplatin will be given once per cycle, on day 1, while gemcitabine is given twice per cycle on days 1 and 8. The first several study participants will receive the lowest dose of M6620 (VX-970) and gemcitabine. If these doses of M6620 (VX-970) and gemcitaibe do not cause serious side effects, the dose of M6620 (VX-970) and gemcitabine will be increased and given to other study participants. The doses of M6620 (VX-970) and gemcitabine will continue to increase for every group of study participants until side effects occur that require the dose to be lowered. This next lower dose is considered to be safe and will be used in the next part of the study. At this time, patient enrollment into the phase 1 part of the study is stopped.

Drug	Route	Length of IV infusion	Days given during cycle
Carboplatin	IV	30 minutes	1
Gemcitabine	IV	30 minutes	1 and 8
M6620 (VX-970)	IV	60 minutes	2 and 9

The study medication M6620 (VX-970) has the potential to interact with other medications; you will be given a drug interaction handout and wallet card as a resource for yourself, caregivers and other health care providers.

How long will I be in this study?

During the study, you may continue to receive treatment with M6620 (VX-970), carboplatin and gemcitabine for an indefinite number of cycles; 'indefinite' means that it is not known exactly how long you will be in this study because each person responds to the study treatment differently.

You may continue to receive treatment as long as your doctor feels the treatment is helping you, you are not having unacceptable side effects or you do not withdraw study consent.

After you finish your treatment, your doctor will continue to watch you for side effects and follow your condition for 3 years. If you are removed from the study for unacceptable side effects, your doctor will continue to monitor you until resolution or stabilization of the side effects.

If your physician notes that your cancer has responded well to the therapy, you may have the option to discontinue the study treatments (carboplatin, gemcitabine and M6620 (VX-970) and start a class of drugs called "PARP inhibitors" that are now FDA approved as maintenance therapy. Your physician will discuss this option with you, so please ask if you have further questions about this option.

What extra tests and procedures will I have if I take part in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. Most of the exams, texts, and procedures you will have are part of the usual approach for your cancer. However, there are some extra procedures that you will need to have if you take part in this study.

You will need to have a blood sample taken for the study. You will have blood draw for research before Cycle 1 Day 2. About four teaspoons (20 mL) of blood will be drawn. Researchers will obtain genetic material (DNA) from your blood samples. You and your study doctor will not get any results of this testing.

A study calendar that shows when and how often the exams, tests and procedures will be done is attached to the end of this consent form.

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

The M6620 (VX-970) used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach. The study drug(s)/study approach may not be better, and could possibly be worse, than the usual approach for your cancer.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.
- The study doctor will provide you with information about other drugs you may need to avoid while receiving the study drug.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of M6620 (VX-970)

POSSIBLE, SOME MAY BE SERIOUS
• Anemia which may require blood transfusion • Diarrhea, nausea, vomiting • Tiredness • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Infection especially when white blood cell count is low which may cause painful and frequent urination • Bruising, bleeding • Pain in tumor • Dizziness, headache • Itching, rash • Flushing

Risk of Increased Sensitivity to Sunlight
There is a possibility that M6620 (VX-970) may make you more sensitive to sunlight. You should limit your exposure to the sun, including indoor tanning. It is recommended to use sunscreen and wear long sleeved clothing, hats, and sunglasses.

Possible Side Effects of Carboplatin

COMMON, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, more than 20 and up to 100 may have:
• 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

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Carboplatin, from 4 to 20 may have:
• 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

RARE, AND SERIOUS In 100 people receiving Carboplatin, 3 or fewer may have:
• Damage to organs which may cause hearing and balance problems

Possible Side Effects of Gemcitabine

COMMON, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, more than 20 and up to 100 may have:
• Flu-like symptoms of muscle pain, fever, headache, chills and fatigue • Nausea, vomiting • Rash • Hair loss • Infection, especially when white blood cell count is low • Bruising, bleeding • Anemia which may require a blood transfusion • Muscle weakness • Blood in urine • Feeling of "pins and needles" in arms and legs

COMMON, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, more than 20 and up to 100 may have:
• Numbness and tingling of the arms and legs • Tiredness • Difficulty sleeping • Hearing loss • Swelling of arms, legs

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Gemcitabine, from 4 to 20 may have:
• Swelling and redness of the area of radiation • Blisters on the skin • Diarrhea, constipation • Sores in mouth which may cause difficulty swallowing • Liver damage which may cause yellowing of eyes and skin, swelling • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Scarring of the lungs • Shortness of breath • Fluid in the organs which may cause low blood pressure, shortness of breath, swelling of ankles • Brain damage, Reversible Posterior Leukoencephalopathy Syndrome, which may cause headache, seizure, blindness

RARE, AND SERIOUS In 100 people receiving Gemcitabine, 3 or fewer may have:
• Severe blood infection • Anemia, kidney problems which may require dialysis • Blood clot • Blockage of the airway which may cause cough

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks for females of child bearing potential: You should not get pregnant or breastfeed a baby while in this study. The M6620 (VX-970), carboplatin and gemcitabine used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study. Use of birth control or pregnancy prevention should continue for 6 months after the end of study treatment. If you become pregnant during study treatment, please notify your doctor immediately.

What possible benefits can I expect from taking part in this study?

This study is unlikely to help you. Researchers hope that the addition of the study drug M6620 (VX-970) to the standard chemotherapy treatment will work better to kill cancer cells compared to the standard chemotherapy alone. This study may help researchers learn things that may help other people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____*(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

The M6620 (VX-970) will be supplied by NCI at no charge while you take part in this study. The cost of getting the M6620 (VX-970) ready and giving it to you is also provided at no charge. It is possible that the M6620 (VX-970) may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You will not need to pay for the blood draw for research or the research tests performed on this blood sample.

You and/or your health plan/insurance company will need to pay for all of the other costs of caring for your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. The cost of carboplatin and gemcitabine as well as the cost of getting the carboplatin and gemcitabine ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require

doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Vertex Pharmaceuticals or any drug company supporting the study
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration in the U.S. and similar ones if other countries are involved in the study.
- The National Cancer Institute will obtain information from this clinical trial under data collection authority Title 42 U.S.C. 285.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s] to be contacted))* at _____ *(insert telephone number).*

My Signature Agreeing to Take Part in the Phase 1 Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the phase 1 study.

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____

Study Calendar

Visit	Patient Activities
Pre-Study	**Within 21 days of registration** • Informed consent • Physical exam and medical history interview • *For females who may become pregnant only*: Serum pregnancy test **Within 7 days of registration** • Physical exam • Routine blood tests for hematology, chemistry, CA-125 • MRI or CT scan of the abdomen/pelvis **At any time after consent up to Cycle 1 Day 2:** • Blood draw for research
Cycle 1	**Day 1** • Medical history interview • Routine blood tests for hematology, chemistry, CA-125 • Carboplatin and gemcitabine given by IV infusion over about 1 hour **Day 2** • M6620 (VX-970) given by IV infusion over about 1 hour **Day 8** • Routine blood test for hematology • Gemcitabine given by IV infusion over about 30 minutes **Day 9** • M6620 (VX-970) given by IV infusion over about 1 hour
All Subsequent Cycles	**Day 1** • Physical exam and medical history interview • Routine blood tests for hematology, chemistry, CA-125 • Carboplatin and gemcitabine given by IV infusion over about 1 hour **Day 2** • M6620 (VX-970) given by IV infusion over about 1 hour **Day 8**

	• Routine blood test for hematology • Gemcitabine given by IV infusion over about 30 minutes **Day 9** • M6620 (VX-970) given by IV infusion over about 1 hour
At the End of Even Numbered Cycles for 1 year; Then Every 3 Months until the End of the Study	MRI or CT scan of the abdomen/pelvis
Off Treatment	Routine blood tests for hematology, chemistry, CA-125