University of California, Los Angeles

Phase Ib Trial of Pembrolizumab (MK-3475) with Platinum-based Chemotherapy in Small Cell/Neuroendocrine Cancers of Urothelium and Prostate

Principle Investigator: Arnold Chin, M.D.
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University of California, Los Angeles

INFORMED CONSENT FORM FOR MEDICAL RESEARCH

CONSENT TO PARTICIPATE IN RESEARCH

Phase Ib Trial of Pembrolizumab (MK-3475) with Platinum-based Chemotherapy in Small Cell Cancers of Urothelium and Prostate

INTRODUCTION

Arnold I. Chin, MD, PhD and associates from the UCLA Department of Urology at the University of California, Los Angeles are conducting a research study.

The researchers will explain this study to you. **Research studies are voluntary and include only people who choose to take part.** Please take your time about deciding whether to participate in this study.

Before deciding:

- You can discuss this study with friends and family.
- You can also discuss it with your health care doctor or request a second opinion.
- If you have any questions, you can ask the researchers for more information before deciding to participate.

The research team is asking you to be in this study because you have a certain aggressive type of bladder or prostate cancer.

There may be reasons why you are not allowed to take part in this study. The study doctor or staff will discuss these with you.

WHY IS THIS STUDY BEING DONE?

This study is being done to see how the experimental drug, pembrolizumab (also called MK-3475), will work in conjunction with standard of care chemotherapy consisting of etoposide and cisplatin/carboplatin or docetaxel and carboplatin to help people with small cell carcinoma of the urothelial or prostate. This drug is approved in patients with many types of cancer, including certain types of bladder, lung, melanoma, head and neck cancers, and lymphoma.

Your taking part in this study may help to answer the following research question(s):

- The safety and tolerability of pembrolizumab in conjunction with platinum-based chemotherapy.
- The effectiveness of pembrolizumab plus etoposide and cisplatin/carboplatin or docetaxel and carboplatin measured by the rates of response to treatment and survival.

This study is being funded by Merck & Co., Inc.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 15 people will take part in this study across all sites. Approximately 15 people will participate in this study at UCLA.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

Screening Visit

If you agree to participate in this study, you will need to have the following exams, tests, or procedures to find out if you can be in the study, known as screening. These screening evaluations will occur up to 28 days before you begin the study. Some of the exams, tests, or procedures may be part of your regular medical care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor. The study doctor or staff will perform the following tests:

- Collect information about you including your medical history and demographics (including age and race/ethnicity).
- Review your prior and current medications and treatments, including over-the counter and herbal/homeopathic remedies.
- Have your height, weight, and vital signs (heart rate, breathing rate, blood pressure, and temperature) measured.
- Perform a complete physical exam.
- You will be asked how well you carry out daily activities (performance status).
- You will be asked about your current disease related symptoms.
- Perform a computed tomography (CT) scan or magnetic resonance imaging (MRI) scan, and physical examination to measure the size of your tumor. Most areas of your body will be scanned. This will include scans of your chest, abdomen, and pelvis. X-rays may also be done, if needed.
- Collect blood (about 2 tablespoons) for routine safety tests on your blood counts, liver and kidney function, blood sugar, and for other safety tests (must be done within 10 days of Day 1).
- Collect blood or urine for a pregnancy test if you are a female (must be within 10 days of Day 1).
- Collect urine samples for routine safety tests (must be done within 10 days of Day 1).
- You will be asked to provide a cancer sample from a previous biopsy or surgical procedure (taking a tissue sample from your tumor or removal of a tumor). Tumor biopsies may be done as either excisional (entire tumor lesion will be removed), incisional (part of the tumor lesion will be removed), or punch and/or core needle (small sample of tissue will be removed using a needle) taken under radiologic or ultrasound imaging.

This visit requires approximately 6 hours, and sometimes it may be necessary for you to come to the clinic one additional day in order to complete some procedures. A decision about your eligibility to participate will be made when the results from your screening tests and procedures are available.

Study Drug Administration

Pembrolizumab is given as a 30-minute infusion into a vein every 3 weeks.

This will be done in conjunction with intravenous infusion of standard of care chemotherapy for your cancer, including etoposide and cisplatin/carboplatin or docetaxel and carboplatin.

Visits during the study

The following tests and procedures will be performed during the treatment period of the study. Most of these tests and procedures are part of regular medical care, but they may be done more often for this study. Some of the tests will be used to determine if the drug is working, while other tests will be performed to monitor your health and the safety of the study drug. The study visits will require about 2 hours each visit depending on the tests and procedures scheduled. You will be administered the study drugs as described in the section above, "Study Drug Administration".

During the treatment portion of the study, you will come to clinic every 3 weeks.

The following procedures may be done at each study visit.

- Review your symptoms, side effects, or changes to your health
- You will be asked to report any new medications or any changes to the medications you are taking
- You will have a physical exam performed
- Your vital signs and weight will be measured
- Your performance status will be evaluated
- Blood (about 1-2 tablespoons) or urine samples may be taken
- You will be given pembrolizumab through an IV infusion
- You may receive standard of care chemotherapy

In addition to the procedures done at every visit, you may have the following performed at study visits described below.

The following procedures may be done prior to treatment every cycle.

- Research blood (about 1-2 tablespoons) and/or urine samples will be taken. Analyses will be conducted on the blood, including genetic analysis, and urine.

The following procedures will be done initially at 9 weeks, then every 12 weeks thereafter based on the date of the previous scan.

- A CT or MRI scan and/or bone scan will be performed to assess your tumor staging

The following procedure will be done at progression:

- Research blood (about 1-2 tablespoons) and/or urine sample will be taken

Optional Procedures

If you participate in this study, you will be asked to participate in the following optional procedure.

Participating in the optional procedure will help researchers learn more about the way patients respond to the study drug pembrolizumab.

- Tumor tissue biopsy on progression of disease.

The procedure is optional and performed for research only. You may refuse the procedure and still be able to be in the study. If you agree to participate in the optional procedure, you will be asked to select your choice at a later time.

End of treatment and follow-up

When for any reason you stop the study treatment, you will be asked to return to the clinic within 30 days of last taking your study medication. At this End of Treatment visit, the following procedures and assessments will be performed unless they were already performed within 7 days prior to the visit (or 28 days for tumor assessments):

- Review your symptoms, side effects, or changes to your health
- You will be asked to report any new medications or any changes to the medications you are taking.
- Your vital signs and weight will be measured.
- Perform a complete physical exam.
- You will be asked how well you carry out daily activities (performance status).
- Collect blood (about 2-3 tablespoons) for routine safety tests
- A CT or MRI scan will be performed to assess your cancer.
- A fresh tumor biopsy sample will be collected if you agree to provide it.

Additionally, the following procedures will be done every 12 weeks based on the date of the previous scan, until 2 years from start of treatment.

- A CT or MRI scan and/or bone scan will be performed to assess your tumor

Once a subject completes the follow-up visits, the subject moves into the survival follow-up phase with a telephone call every 12 weeks.

HOW LONG WILL I BE IN THIS STUDY?

You will be in the study as long as your disease is not getting worse and you do not have bad side effects for up to 2 years. You will continue to receive study treatment until your doctor has determined that your cancer has progressed, until the study treatment becomes intolerable, or until the completion or termination of the study. If you continue to benefit after 2 years, you may be eligible for an additional year of treatment.

WHAT KINDS OF RISKS OR DISCOMFORTS COULD I EXPECT?

What is known about this study drug?

Pembrolizumab, which is approved in the USA and some other countries, is available by prescription to treat several different cancers, but may not be approved to treat your type of cancer.

Pembrolizumab 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. These side effects can affect more than one of your normal organs and tissues at the same time.

What side effects could the study drug(s) cause?

VERY COMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life threatening or where noted, may cause death)

Out of 100 people who receive pembrolizumab, 20 or more people may have the following:

- Itching of the skin
- Loose or watery stools
- Cough

COMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life-threatening, or where noted, may cause death)

Out of 100 people who receive pembrolizumab, at least 5 but less than 20 people may have the following:

- Joint pain
- Rash
- Fever
- Back pain
- Pain in your belly
- Loss of skin color
- Not enough thyroid hormone so you may feel tired, gain weight, feel cold, have infrequent or hard stools (Hypothyroidism)
- Low levels of salt in the blood that may cause you to feel tired, feel confused, have a headache, have muscle cramps and/or feel sick to your stomach (Hyponatremia)

UNCOMMON, SOME MAY BE SERIOUS (i.e. causing hospitalization, life threatening, or where noted, may cause death)

Out of 100 people who receive pembrolizumab, at least 1 but less than 5 people may have the following:

- Inflammation of the lungs so you may feel short of breath and cough (pneumonitis)

- Too much thyroid hormone so you may feel anxious, feel angry, have trouble sleeping, feel weak, tremble, sweat, feel tired, have loose and watery stools (hyperthyroidism)
- Infusion reaction, where you may feel dizzy or faint, feel flushed, get a rash, have a fever, feel short of breath, experience a decrease in your blood pressure at the time of receiving your infusion (IV) or just after, or have pain at the site of infusion
- Inflammation of the bowels/gut, which may cause severe pain in your belly with loose or watery stools, and black, tarry, sticky stools or stools with blood or mucus (colitis)
- Inflammation of the skin so you may have peeling of the skin, itchiness, and/or skin redness. The skin inflammation (i.e. peeling, itching and redness) could also be widespread throughout your body. More severe skin reactions may involve the inside of your mouth, the surface of your eye and genital areas, and/or may cause the top layer of your skin to peel from all over your body which can cause severe infection(Severe skin reactions, including Stevens-Johnson syndrome or toxic epidermal necrolysis)

RARE, SOME MAY BE SERIOUS (i.e. causing hospitalization, life-threatening, or where noted, may cause death)

Out of 100 people who receive pembrolizumab, less than 1 person may have the following:

- Inflammation of the nerves that may cause pain, weakness or tingling in your hands and feet, and may spread to your legs, arms and upper body leading to severe muscle weakness and possible temporary paralysis (Guillain-Barré syndrome)□
- Inflammation of the muscles so you may feel weak or have pain in your muscles (Myositis)
- Inflammation of the pancreas (a gland in your abdomen that controls sugar levels) so you may have severe pain in the top part of your belly that may move to your back, feel sick to your stomach, and vomiting that gets worse when you eat (pancreatitis)
- Inflammation of the eye so you may have eye redness, blurred vision, sensitivity to light, eye pain, see floaters or have headaches (uveitis)
- Inflammation of the liver that may make you feel sick to your stomach and vomit, feel like not eating, feel tired, have a mild fever, have a pain in the right side of your belly, yellow eyes and skin, and dark urine (hepatitis)
- Inflammation of the pituitary gland (a gland in the head), which may cause you to feel sick to your stomach or have headaches, changes in your behavior, double vision, few to no menstrual cycles, weakness, vomiting and dizziness or fainting (hypophysitis)
- Adrenal glands (glands on top of the kidneys) that may not make enough hormone, which could cause tiredness, weight loss, muscle weakness, feeling faint, joint, muscle and belly aches, nausea, vomiting, loose or watery stools, fever, salt craving, and sometimes darkening of the skin like a suntan (adrenal insufficiency)
- Type 1 Diabetes, a condition that can cause too much sugar in your blood, feeling thirstier than usual, frequent urination and weight loss. You are likely to need regular insulin shots
- Inflammation of the kidney so you may pass less urine or have cloudy or bloody urine, swelling and low back pain (nephritis)
- Inflammation of the middle layer of your heart wall that may cause your heart to have difficulty pumping blood throughout your body, which can cause chest pain, shortness of breath and swelling of the legs. You may experience a fast or irregular heartbeat that may cause dizziness or fainting (myocarditis)

- Inflammation of the thyroid gland, an organ that makes and stores thyroid hormones. This condition may lead to change in your heart rate, blood pressure, body temperature, and the rate at which food is converted into energy (thyroiditis)
- A condition that may make you feel weak and tired and might have drooping of the eyelids, blurred or double vision, difficulty swallowing, slurred speech, weakness in your arms and legs, or difficulty breathing
- The formation of small clusters of immune cells (called granulomas) in parts of your body such as your lymph nodes, eyes, skin, or lungs (sarcoiditis)
- Inflammation of the brain with confusion and fever. This may also include: disorientation, memory problems, seizures (fits), changes in personality and behavior, difficulty speaking, weakness or loss of movement in some parts of your body, and loss of consciousness (encephalitis)
- Inflammation of the spinal cord with pain, numbness, tingling, or weakness in the arms or legs, bladder or bowel problems including needing to urinate more frequently, urinary incontinence, difficulty urinating, and constipation (myelitis)
- Inflammation of the blood vessels (vasculitis). 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.

Additionally, since pembrolizumab was approved in September 2014, the following side effects have been reported by people receiving pembrolizumab. These side effects were voluntarily reported from a group of people of unknown size. It is not possible to estimate the frequency of these side effect:

- Inflammation of the joints which may include joint pain, stiffness and/or swelling (arthritis)
- Severe responses of the immune system that cause the body to attack its own blood cells, spleen, liver, lymph nodes, skin and brain. This may include fever, rash, inflammation of the liver, yellowing of the skin, an enlarged liver and spleen, low blood counts, and enlarged lymph nodes. The nervous system may also be affected and cause confusion, seizures, and even coma (hemophagocytic lymphohistiocytosis)
- Changes in eyesight, eye pain, whitish patches on the skin and hearing loss (Vogt-Koyanagi-Harada syndrome)
- Inflammation and scarring of the bile ducts (tubes that carry digestive fluid that is made in the liver). This can cause symptoms similar to those seen with inflammation of the liver (hepatitis) such as pain in right side of your belly, yellow eyes and skin, feeling tired, and itching (sclerosing cholangitis).

In addition to the above, if you have had an allogeneic stem cell transplant (a procedure in which a person receives blood-forming stem cells from a donor), you may experience graft versus host disease (GvHD), which may include diarrhea, skin rashes, and liver damage, after receiving pembrolizumab. Sometimes this condition can lead to death.

Risks of Chemotherapy: Etoposide, Cisplatin, Carboplatin, Docetaxel
The risks of standard of care chemotherapy consisting of etoposide and cisplatin/carboplatin or docetaxel and carboplatin are described in the Appendix. These are treatments you might receive without participation in this study.

Blood draw risks
Drawing blood may cause temporary pain from the needle stick, bruising or swelling at the site, and rarely, infection or fainting.

Tumor Biopsy
A biopsy means taking some cells from inside your bones or soft tissue. An area of your skin will be numbed with a shot. This shot may cause a little pain. Some people (fewer than 1 in 10,000) are allergic to the numbing shot. Then, a long needle will be inserted into your bone or soft tissue to get the sample. Some people have moderate to severe pain with this procedure. The area of the biopsy may hurt for about 3-6 days. There is a small chance you will get a bruise or an infection where the needle will be inserted. You may bleed or have a scar. Your skin may itch. These problems are rare. The risks will be different based upon the site where the biopsy is taken and potential side effects will be described to you by the radiologist before the procedure is performed.

Radiation Exposure
You are exposed to radiation on a daily basis, both from natural (sun and earth) and manmade sources. The estimated radiation dose that you will receive as a volunteer for this type of research has been compared to the limits allowed for a radiation worker. This limit is not expected to be harmful. The person obtaining your consent can answer any questions you have, and provide detailed written information about the amount of radiation resulting from this study.

CT scan risks
CT scans involve the risks of radiation (see above). In addition, if contrast material (iodine dye) is used, there is a slight risk of developing an allergic reaction, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock, or rarely, death. The contrast material may also cause kidney problems, especially if you are dehydrated or have poor kidney function. The study doctors will ask you about any allergies or related conditions before the procedure. If you have any of these problems, you may not be allowed to have a CT scan or continue in the study.

Having a CT scan may mean some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner, or by lying in one position for a long time. If contrast material is used, you may feel discomfort when it is injected. You may feel warm and flushed and get a metallic taste in your mouth. Rarely, the contrast material may cause nausea, vomiting or a headache.

MRI risks
The MRI procedure uses a powerful magnetic field to generate detailed images of the body. The magnet could move objects within your body that contain metal, such as implants, clips and pacemakers. Tell the doctor if you have any metal items within your body.

MRI scanning is painless but you might experience discomfort in the machine. In particular, loud beeping and hammering noises occur during the study when the scanner is collecting measurements. You also may be bothered by feelings of claustrophobia when placed inside the MRI, or by lying in one position for a long time. You might also experience stimulation of the nerves in your body, which feels like a gentle tap or sensation of mild electric shock.

Injection of Gadolinium during Clinical MRI
Gadolinium, a substance given during the MRI examination, will be given by injection into a vein in your arm. This may cause some minor pain, and may cause some bruising near the area of injection. Gadolinium may also cause headache, nausea, and vomiting. Rarely, it may cause dizziness, rash, itching, or a numb or tingling feeling in the hands or feet, or an allergic reaction. Medical personnel will be available to treat any of these problems if they should occur.

Nephrogenic Systemic Fibrosis Risk Associated with Gadolinium
Some people who have had MRIs with gadolinium-based contrast agent gadodiamide have experienced a serious reaction called nephrogenic systemic fibrosis (NSF). NSF is a condition where people develop large areas of hardened skin with lesions called plaques and papules with or without skin discoloration. In some cases, NSF could lead to physical disability and may involve not only the skin, but also the liver, lungs, muscles and heart. The typical patient in whom this has occurred is middle-aged and has end-stage kidney disease.

Gadolinium Retention in Brain Tissue
Some people who have had four or more MRIs with gadolinium-based contrast agents experienced trace amounts of gadolinium being retained in their brain long after the last MRI. It is unknown whether these gadolinium deposits are harmful or can lead to adverse health effects.

Reproductive risks
You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study, even if you cannot father a child. It is recommended that if you are sexually active, you use a condom while on this study and for at least 30 days after you stop taking the study drugs. If you are able to father a baby, it is recommended that you use a condom and a second method of birth control while on this study and for at least 6 months after you stop taking the study drugs. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

Unknown Risks to Women of Child Bearing Potential and Pregnant Women
The effects of the study drug on fertility or a fetus are not known. For this reason, if you believe that you are pregnant or have a chance of becoming pregnant you should not participate in this study. A blood or urine pregnancy test will be performed before the start of study procedures. If you are pregnant, you will not be allowed to participate in the study. If you do participate in this study, you must use a medically effective form of birth control before entering the study, while participating in the study, and for at

least 30 days after stopping the study. If you become pregnant during the study, tell the researchers right away.

Unknown risks and discomforts
The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

ARE THERE ANY BENEFITS IF I PARTICIPATE?

Possible benefits to me
You may or may not benefit from taking part in this study.

Possible benefits to others or society
Information learned from the study may help other people in the future.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?

You may wish to talk with your treating physician about your choices before deciding if you will take part in this study.

If you decide not to participate in this study, your other choices may include:

- Receiving chemotherapy alone.
- Receiving no treatment at this time.
- Taking part in another study.
- Receiving comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems, and other problems caused by your disease. It does not treat the diseases directly, but instead tried to improve how you fell. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide whether you will take part in this study. If you choose not to participate in this study, it will not affect the other options available to you.

During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.

CAN THE RESEARCHERS REMOVE ME FROM THIS STUDY?

The researchers may end your participation in this study for a number of reasons, such as if your safety and welfare are at risk, if you do not follow instructions or if you miss scheduled visits. The researchers or the study sponsor might also decide to stop the study at any time.

If you decide to stop being in the study, or are removed from the study, or the study is stopped the

researcher will ask you to return to clinic after your last study drug dose for follow-up test and procedures as described within the "Visits after your last dose of study drug" section of this form. The data collected about you up to the point of withdrawal will remain part of the study and may not be removed from the study database.

You may decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. The study doctor will tell you how to stop safely.

If you are participating in the optional procedures, you can decide to stop at any time. If you change your mind, tell your study doctor that you no longer want your tissue sample to be used for research. Then, any blood or tissue samples that remain will be destroyed. You do not need to give a reason for changing your mind. If you change your mind, and your samples have already been tested, those results will still remain part of the overall research data.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?

The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but participating in research may involve a loss of privacy and the potential for a breach in confidentiality. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. The research team will carefully follow the coding, storage, and data sharing plan explained below.

You will be asked to sign a separate form called the **University of California Permission to Use Personal Health Information for Research** that will allow UCLA to share information from your medical records with the study doctor so they can use your information as part of this study.

Use of personal information that can identify you:
All identifiable information about you will be replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data.

How information about you will be stored:
Some research data and records will be maintained in a secure location at UCLA. Only authorized individuals will have access to it. Other research data and records will be stored electronically on a secure network with encryption and/or password protection.

People and agencies that will have access to your information:
The research team, authorized UCLA personnel, the institutional review board responsible for protecting the rights and safety of the patients who take part in research studies, and regulatory agencies such as the Food and Drug Administration (FDA), may have access to study data and records to monitor the study. Research records provided to authorized, non-UCLA personnel will not contain identifiable information about you. Publications and/or presentations that result from this study will not identify you by name.

In the event of an unexpected breach of confidentiality, a federal law called the Genetic

Information Non-Discrimination Act (GINA) will help protect you from health insurance or employment discrimination based on genetic information obtained about you. In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

ARE THERE ANY COSTS FOR TAKING PART IN THIS STUDY?

The study will pay for research-related items and/or services that are provided only because you are participating in the study. These research-related items and/or services are explained in other areas of this consent form.

You or your health plan may be responsible to pay for all the types of items listed below:

- Items and services that would have been provided to you even if you were not in the study
- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items and/or services

WILL I BE PAID FOR MY PARTICIPATION?

You will not be paid to be in this study. If you incur parking fees on days where the main purpose of your visit is research related, the costs of parking will be reimbursed.

WHAT OTHER THINGS SHOULD I CONSIDER BEFORE PARTICIPATION?

Use of My Specimens:
Any specimens (e.g., tissue, blood, urine, tumor sample) obtained for the purposes of this study will be provided to the Sponsor of this study. These specimens will not include information that identifies you directly. Once you provide the specimens you will not have access to them. The specimens will be used for research and such use may result in discoveries, developments, or inventions that could become the basis for new products or therapeutic agents. In some instances, these discoveries may be of potential commercial value. You will not receive any money or other benefits derived from such a product.

It may take many years to complete this research, so your samples will be stored indefinitely or until they are all used up. Your tissue and related medical information will be used only for research and will not be sold. Your samples will not be used for research involving human cloning (growing human tissue from this material). Information from this research will be from all the patients who participate in this study as a group, not just from your samples.

Withdrawing of specimens and data by the research participant:
If you want to withdraw from this research study you can contact Dr. Arnold I. Chin, He will contact the study sponsor to destroy any remaining specimens of yours that have been obtained for the study.

You may withdraw from the optional procedures by informing the study doctor. You can withdraw from the optional procedures and continue participation in the main study.

However, the samples and data generated from your specimens that have already been used cannot be withdrawn.

WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team:

You may contact the investigators below with any questions or concerns about the research or your participation in this study. You can also call the UCLA Page Operator at (310) 825-6301 to reach any of the investigators below 24 hours a day, 7 days a week.

Principal Investigator
[redacted] Chin, MD, PhD
Associate Professor of Urology
[redacted]

UCLA Study Team
[redacted] Drakaki, MD, PhD
Assistant Professor of Hematology and Oncology
[redacted]

[redacted] Liu, MD
Assistant Professor of Hematology and Oncology
[redacted]

[redacted] Rettig, MD
Professor of Hematology and Oncology
[redacted]

[redacted] Shen, MD
Assistant Professor of Hematology and Oncology
[redacted]

UCLA Office of the Human Research Protection Program (OHRPP):
If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, you may contact the UCLA OHRPP by phone: (310) 825-5344; by email: mirb@research.ucla.edu or U.S. mail: UCLA OHRPP, 10889 Wilshire Blvd., Suite 830, Los Angeles, CA 90095.

Public Information about this Study:
ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most,

the website will include a summary of the results. You can search this website at any time.

WHAT HAPPENS IF I BELIEVE I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number(s) listed above.

If you are injured as a result of being in this study, UCLA will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor, or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call the UCLA Office of the Human Research Protection Program at 310-825-5344 or send an email to mirb@research.ucla.edu.

WHERE CAN I GET MORE INFORMATION ABOUT PARTICIPATING IN CLINICAL TRIALS?

National Cancer Institute Information:

The National Cancer Institute's (NCI) Clinical Trials Reporting Program (CTRP) is a comprehensive database of information about all NCI-supported clinical trials. The goal of this comprehensive database is to help NCI identify areas that need more clinical research and to help NCI decide which studies are most important to do first. The NCI requires that cancer clinical trials report information about how many subjects are enrolled in the trials and the outcome of the trials. Specific information about you as a subject will be included in the database. This information will include information about your cancer, your study identification number, the month and year of your birth, as well as your gender, country of origin, race, ethnicity, and zip code. This information will be maintained in a secure and confidential manner by the NCI CTRP in their electronic database. The NCI CTRP has many safeguards in place for privacy, security, and limited authorized access.

You may call the National Cancer Institute's Cancer Information Service at:

- 1-800-4-CANCER (1-800-422-6237) or DSTTY: 1-800-332-8615

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

WHAT ARE MY RIGHTS IF I TAKE PART IN THIS STUDY?

Taking part in this study is your choice. You can choose whether or not you want to participate. Whatever decision you make, there will be no penalty to you and you will not lose any of your regular benefits.

- You have a right to have all of your questions answered before deciding whether to take part.
- Your decision will not affect the medical care you receive from UCLA.
- If you decide to take part, you can leave the study at any time.
- If you decide to stop being in this study you should notify the research team right away. The researchers may ask you to complete some procedures in order to protect your safety.
- If you decide not to take part, you can still get medical care from UCLA.

HOW DO I INDICATE MY AGREEMENT TO PARTICIPATE?

If you agree to participate in this study you should sign and date below. You have been given a copy of this consent form and the Research Participant's Bill of Rights to keep. You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

- **FUTURE USE OF DATA AND/OR SPECIMENS**

Please check the appropriate box below and initial:

☐ I agree to have my data/specimens stored for future use by the Principal Investigator and/or research team. Initials _____

☐ I do not want my data/specimens stored for future use by the Principal Investigator and/or research team. Initials _____

- **SHARING OF SAMPLES**

Please check the appropriate box below and initial:

☐ I agree to have my tissue/fluid sample shared with other researchers. Initials _____

☐ I do not want my tissue/fluid sample shared with other researchers. Initials _____

SIGNATURE OF THE PARTICIPANT

_____
Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF PERSON OBTAINING CONSENT

_____ _____
Name of Person Obtaining Consent Contact Number

_____ _____
Signature of Person Obtaining Consent Date

Appendix

Risks of Etoposide

More common

- Black, tarry stools
- bleeding gums
- blood in the urine or stools
- chest pain
- chills
- cough
- fever
- painful or difficult urination
- pale skin
- pinpoint red spots on the skin
- shortness of breath
- sore throat
- sores, ulcers, or white spots on the lips or in the mouth
- swollen glands
- troubled breathing with exertion
- unusual bleeding or bruising
- unusual tiredness or weakness

Less common

- Blurred vision
- confusion
- cough or hoarseness, accompanied by fever or chills
- difficulty with swallowing
- dizziness
- dizziness, faintness, or lightheadedness when getting up suddenly from a lying or sitting position
- face is warm or hot to touch
- fast heartbeat
- headache
- hives, itching, or skin rash
- lower back or side pain, accompanied by fever or chills
- nervousness
- numbness or tingling in the fingers or toes
- pain or redness at the site of injection
- pale skin at the site of injection
- pounding in the ears
- puffiness or swelling of the eyelids or around the eyes, face, lips, or tongue
- redness to face
- slow or fast heartbeat
- sweating

- tightness in the chest

Rare

- Back pain
- difficulty with walking
- loss of consciousness
- swelling of the face or tongue
- tightness in the throat

Incidence not known

- Abdominal or stomach pain, severe
- blindness
- blistering, peeling, or loosening of the skin
- blue-yellow color blindness
- dark urine
- decreased vision
- eye pain
- joint or muscle pain
- loss of appetite
- nausea or vomiting
- red, irritated eyes
- red skin lesions, often with a purple center
- seizures
- yellow eyes or skin

Some side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects. Check with your health care professional if any of the following side effects continue or are bothersome or if you have any questions about them:

More common

- Bad, unusual, or unpleasant (after) taste
- change in taste
- constipation
- cracked lips
- hair loss or thinning of the hair
- lack or loss of strength
- swelling or inflammation of the mouth
- weight loss

This medicine often causes a temporary loss of hair. After treatment with etoposide has ended, normal hair growth should return.

Other side effects not listed may also occur in some patients. If you notice any other effects, check with your healthcare professional.

Risks of Cisplatin

Check with your doctor immediately if any of the following side effects occur:

Less common

- Black, tarry stools
- blood in urine or stools
- cough or hoarseness accompanied by fever or chills
- dizziness or faintness (during or shortly after a dose)
- fast heartbeat (during or shortly after a dose)
- fever or chills
- lower back or side pain accompanied by fever or chills
- painful or difficult urination accompanied by fever or chills
- pain or redness at place of injection
- pinpoint red spots on skin
- swelling of face (during or shortly after a dose)
- unusual bleeding or bruising
- wheezing (during or shortly after a dose)

Check with your doctor as soon as possible if any of the following side effects occur:

More common

- Joint pain
- loss of balance
- ringing in ears
- swelling of feet or lower legs
- trouble in hearing
- unusual tiredness or weakness

Less common

- Convulsions (seizures)
- loss of reflexes
- loss of taste
- numbness or tingling in fingers or toes
- trouble in walking

Rare

- Agitation or confusion
- blurred vision
- change in ability to see colors (especially blue or yellow)
- muscle cramps
- sores in mouth and on lips

Some side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects.

Check with your health care professional if any of the following side effects continue or are bothersome or if you have any questions about them:

More common
- Nausea and vomiting (severe)

Less common
- Loss of appetite

After you stop using this medicine, it may still produce some side effects that need attention.

Risks of Docetaxel

More common
- Burning, numbness, tingling, or pain in the arms, hands, legs, or feet
- swelling of the stomach, face, fingers, hands, feet, or lower legs
- unusual tiredness or weakness
- weight gain

Less common
- Black, tarry stools
- blood in the urine or stools
- cough or hoarseness (accompanied by fever or chills)
- difficult or labored breathing
- difficult or painful urination (accompanied by fever or chills)
- difficulty with swallowing
- dizziness
- fast heartbeat
- fever or chills
- hives or skin rash
- itching, puffiness, or swelling of the eyelids or around the eyes, face, lips, or tongue
- lower back or side pain (accompanied by fever or chills)
- noisy, rattling breathing
- pinpoint red spots on the skin
- red, scaly, swollen, or peeling areas of the skin (severe)
- tightness in the chest
- troubled breathing while at rest
- unusual bleeding or bruising

Rare
- Chest pain or discomfort
- decreased blood pressure
- fast or irregular heartbeat
- increased blood pressure

Some side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects. Check with your health care professional if any of the following side effects continue or are bothersome or if you have any questions about them:

More common

- Congestion
- diarrhea
- dryness or soreness of the throat
- nausea
- skin rash or redness (mild)
- sores or ulcers on the lips or tongue or inside the mouth
- weakness in the arms, hands, legs, or feet

Less common

- Bloody nose
- body aches or pain
- change in the color of the fingernails or toenails
- dry, red, hot, or irritated skin at the injection site
- headache
- hoarseness
- loosening or loss of the fingernails or toenails, sometimes painful
- pain in the joints or muscles
- pain, swelling, or lump under the skin at the injection site
- runny nose
- tender, swollen glands in the neck
- voice changes
- vomiting

Incidence not known

- Burning, dry, or itching eyes
- burning upper abdominal or stomach pain
- confusion
- difficulty having a bowel movement (stool)
- discharge from the eyes
- excessive tearing
- pain and redness of the skin at the place of earlier radiation treatment
- rapid breathing
- redness, pain, or swelling of the eye, eyelid, or inner lining of the eyelid
- sunken eyes
- tearing of the eyes
- wrinkled skin

Other side effects not listed may also occur in some patients. If you notice any other effects, check with your healthcare professional.

Risks of Carboplatin

More common

- Pain at place of injection

Less common

- Black, tarry stools
- blood in urine or stools
- cough or hoarseness, accompanied by fever or chills
- fever or chills
- lower back or side pain, accompanied by fever or chills
- numbness or tingling in fingers or toes
- painful or difficult urination, accompanied by fever or chills
- pinpoint red spots on skin
- skin rash or itching
- unusual bleeding or bruising
- unusual tiredness or weakness

Rare

- Blurred vision
- ringing in ears
- sores in mouth and on lips
- wheezing

Some side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects. Check with your health care professional if any of the following side effects continue or are bothersome or if you have any questions about them:

More common

- Nausea and vomiting
- unusual tiredness or weakness

Less common

- Constipation or diarrhea
- loss of appetite

This medicine may cause a temporary loss of hair in some people. After treatment with carboplatin has ended, normal hair growth should return. Other side effects not listed may also occur in some patients. If you notice any other effects, check with your healthcare professional.