Document Coversheet

Study Title: A Phase 1 Trial: Porfimer Sodium Mediated Interstitial Photodynamic for the Treatment of Patients with Locally Advanced or Recurrent Head and Neck Cancer

Institution/Site:	Roswell Park Comprehensive Cancer Center
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ROSWELL PARK CANCER INSTITUTE
d/b/a ROSWELL PARK COMPREHENSIVE CANCER CENTER
ELM AND CARLTON STREETS
BUFFALO, NY 14263

Title: A Randomized, Phase 2 Trial with a Phase 1 Safety Run-In: Porfimer Sodium Mediated Interstitial Photodynamic Therapy and Standard of Care Therapy versus Standard of Care Therapy alone for the Treatment of Patients with Locally Advanced or Recurrent Head and Neck Cancer.

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Roswell Park Study Number: I 67918

Consent Form Given to Patient Taking Part in an Investigational/Clinical Research Study

This is a clinical research study. Clinical research studies include only those patients who choose to take part. Please take your time to make your decision. Discuss it with your family and with people who are important to you.

We invite you to take part in a clinical research/investigational study for patients with head and neck cancer.

It is important that you read and understand several general rules that apply to anyone that takes part in our studies:

1. This study is considered research. It is investigational.
2. Taking part in the study is voluntary.
3. You may withdraw from the study at any time without penalty, loss of any benefits or access to care at Roswell Park to which you are otherwise entitled.
4. If you should decide not to take part in this study, it will not affect your care at Roswell Park now or in the future.
5. You should feel free to get a second opinion. This will not affect your ability to receive care and treatment here if you get one.
6. Your disease may not be helped from taking part in this study, but we may get information that will help others.
7. If we become aware of important new findings that relate to your participation or continued participation in this study we will discuss them with you.

The type of study, the risks, benefits, discomforts, and other important information about this study are discussed below.

CONFLICT OF INTEREST STATEMENT

Dr. Gal Shafirstein, D.Sc. (Co-Investigator) is an inventor of a device (light dosimetry system) that will be used in this experimental treatment and for which a patent was filed by the institution. If the patent is pursued, based on data from this and other research, royalties and other compensation may be received by the institution and the investigator. Thus, Roswell Park and the investigator have a financial interest in the outcome of this treatment. Dr. Shafirstein had a paid relationship with the provider of the photodynamic therapy drug (Photofrin®), Pinnacle Biologics, for serving as a member of their advisory board. The drug company also provides drug and research funds to the institution (Roswell Park) for use in research in Dr. Shafirstein's laboratory.

If you require further information regarding the financial arrangements described in this paragraph, you should discuss the matter with the investigator, Dr. Kimberly Wooten, MD at phone number 716-845- 4094.

- Any questions regarding financial conflict issues can be directed to your doctor or to Donald Handley, Executive Director of Research Subject Protection, who can be reached at 716-845-3455.
- This disclosure is made so that you can decide if this relationship will affect your willingness to participate in this study.

1. INTRODUCTION

You are invited to participate in this study because you were diagnosed with head and neck cancer that failed prior treatments, and you are not a candidate for surgery or radiation therapy. To date, the U.S. Food and Drug Administration (FDA) approved to treat tumors like yours with combination chemotherapy and/or targeted therapy and/or immunotherapy, which we call standard of care. Additionally, patient may receive other clinically approved treatments for the disease management that include reirradiation and/or palliative treatment for pain control. However, these standard of care therapies are effective in only about 5% to 15% of the cases and have shown to help in reducing symptoms (palliation) in no more than 36% of the cases. In this study, the doctors assume that they can further improve these cure rates by adding an experimental interstitial photodynamic therapy with porfimer sodium (trade name Photofrin®) to the FDA approved standard of care.

PDT consists of injecting a light sensitive drug (photosensitizer, in this study porfimer sodium) into your vein, waiting for a period of time (about 48 hrs), and then activating the drug with a laser light. Typically the laser light is delivered to the surface of the tumor. However, in the treatment of large cancer tumors (like yours) we must deliver the light through laser fibers that are inserted into the tumor (interstitially). That type of treatment is called interstitial photodynamic therapy (I-PDT).

The FDA has approved the use of porfimer sodium with photodynamic therapy (PDT) in the treatment of early stage cancer of the lung and esophagus, only. Many, small, clinical studies suggest that porfimer sodium with PDT may be beneficial in the treatment of other cancers such as: cancer of the head or neck, various types of skin cancer (excluding melanoma), cancer of the bladder, prostate cancer, breast cancer, vulvar cancer, pancreatic cancer, biliary cancer, and brain cancer. The PDT treatment can be used in combination with surgery and chemotherapy.

In addition, few other clinical studies suggest that adding experimental Photofrin® PDT prior to or during standard of care chemotherapy has the potential to improve outcomes in patients with malignant mesothelioma, advanced esophageal cancer, and for patients with unresectable (cancer that cannot be operated on) cholangiocarcinoma, all of whom have no effective standard treatments.

2. WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to find out if porfimer sodium I-PDT with standard of care is safe and effective to treat patients with head and neck cancer that failed prior treatments and are not candidate to surgery or radiation therapy. Therefore, in this study the doctors' goals are to find answers to the following questions:

1. What is the safest shortest time (between 7(±2) days, 14 (±4) days, or 28 (±4) days) to administer porfimer sodium I-PDT prior to standard of care?
2. How effective porfimer sodium I-PDT with standard of care in comparison to standard of care alone?

To find an answer to the first question the doctors suggest conducting a small study (Phase 1). In this study the doctors will evaluate the safety of I-PDT + standard of care by examining side effects as function of the time (0, 2 or 4 weeks) of when the I-PDT will be administered prior to standard of care.

To find an answer to the second question, the doctors suggest conducting a larger study (Phase 2) where they will compare the objective tumor response (change in tumor size) between the experimental treatment group (I-PDT + standard of care) and standard of care therapy group.

3. WHO ELSE WILL BE ON THIS STUDY AND HOW LONG WILL IT LAST?

In the Phase 1 study up to 12 patients will be enrolled and treated by the doctors at the Roswell Park Comprehensive Cancer Center. The study is expected to enroll patients for 3 years. You will be on the study up to 8 weeks.

4. WHAT WILL HAPPEN IF YOU ARE ON THE STUDY?

Prior to being enrolled you will have to undergo a standard diagnostic head and neck scan with computed tomography (CT) or magnetic resonance imaging (MRI), as clinically indicated. This requirement may be waived if you had such an imaging within 4 weeks prior to entering study, and the study team can receive and evaluate those scans.

Phase 1:

- I-PDT with porfimer sodium prior to your schedule standard of care therapy.
- Standard of Care treatment received at either 7(±2) days, 14 (±4) days, or 28 (±4) days after I-PDT.
    - If your treating physician believes that your tumor may require more than one course of I-PDT for complete and effective illumination, the Standard of care will occur at either 7(±2) days, 14 (±4) days, or 28 (±4) days after your last I-PDT treatment.

The Phase 2 study will begin after the Phase 1 is completed, and the doctors determined the safest time to administer the I-PDT prior to standard of care. Phase 2 will be a randomized research study that will include up to 70 patients from whom 35 will receive I-PDT + Standard of Care, and the other 35 will receive standard of care alone. The doctors at the Roswell Park will treat these patients. You will be on the study up to 2 years. The study should be completed within 2-3 years.

The placement into one of the treatment groups would be random (by chance). Neither you nor your doctor can choose the group that you will be placed in. Randomization is a process used to place patients in different treatment groups. A statistician will use a computer to assign participants to the study groups. By using randomization, the groups will be similar and the treatments they receive can be compared objectively.

You will have same chance of being placed in the I-PDT + standard of care group or in the standard of care group alone. At the time of this study, it is not known which of the treatments is better.

The standard of care treatment will be determined and managed by your Oncologist who will choose the most appropriate FDA approved treatment for you and your disease. The standard of care therapies may include chemotherapy and/or targeted therapy and/or immunotherapy.

Phase 2 you will receive EITHER:

- I-PDT with standard of care therapy
  OR
- Standard of Care treatment only

For either treatment you are randomized to you will be asked to do the following:

- Visit the clinic at approximately 6-8 weeks, and every 3-4 months for year one, and every 4-6 months for year 2, as part of the study.
- Complete a quality-of-life questionnaire prior to treatment and during clinic visits.
- Allow Roswell Park to follow up on your medical condition for 5 years to look at the long-term effects of the treatment/procedure you will receive on the study.

5. IF YOU TAKE PART IN THIS STUDY, WHAT TESTS AND PROCEDURES WILL YOU HAVE DONE?

The doctor will discuss the use of the devices with you and their potential benefits and risks. A brief summary of the experimental treatment may be provided to the company (Pinnacle Biologics, Inc.) to document the use of the dosimetry (measurement) system with the use of the drug and laser. Information the manufacturer may receive about your experimental treatment will contain no information to identify you as an individual.

Which test/procedures (or combination) are considered investigational?

Procedure/Tests	**Where will this be performed? Inpatient Or Outpatient**	**When?**
Computer based treatment planning	Research laboratory	About 3 -28 days prior to the I-PDT
Quality of Life Questionnaire	Outpatient or may complete this at home	Before treatment, at 6-8 weeks and every 3-4 months in the first year post treatment, and every 6 months up to 24 months after treatment.
Insertion of sharp closed-end sterile catheters into the tumor and treatment region	In the operating room	Before light treatment
Experimental laser systems	In the operating room	During light treatment
Treatment laser fibers	In the operating room	During light treatment
Measurement of light dose (part of the dosimetry system)	In the operating room	During light treatment
Use of light detectors (part of the dosimetry system)	In the operating room	During light treatment
I-PDT	In the operating room Outpatient or Inpatient, may be kept for observation	4-24 hours dependent on size of tumor and whether you will be observed for 24 hours
CT or MRI, as clinically indicated	Outpatient	Within 4 weeks before I-PDT.
Use of surface markers	Outpatient	During CT or MR imaging Within 4 weeks before I-PDT
Ultrasound imaging	In the operating room	Before catheters insertion
porfimer sodium (Photofrin®) injection	Outpatient	48 ± 8 hours before the light treatment; you will receive one injection only

The I-PDT with porfimer sodium experimental treatment includes the following steps:

- You will undergo a standard diagnostic head and neck scan with CT or MRI. The doctors, nurse or imaging technician, will place surface markers (temporary stickers) on your skin at the region of the tumor, a few minutes before the imaging. These stickers (about 3-5 mm in diameter) will assist the research team in the planning of the I-PDT. The stickers may be replaced with small points (2-3 mm) of a temporary ink marker. The sticker and ink markers will be removed few minutes before the light treatment. They are not harmful and will leave no permanent mark.
    - If you had a CT or MRI that was obtained within 8 weeks prior to I-PDT, and the

study team can receive the scan for evaluation, then the study team will use that scan and no markers will be placed.

- The scans will be de-identified by removing all your personal details and replacing them with a code that relates to you. The de-identified scans will be sent to Dr. Shafirstein's research laboratory at Roswell Park. Working with your treating physician, Dr. Shafirstein's research team will use a computer code (developed in his laboratory) to generate images and calculate how the laser light will illuminate your tumor. This plan will assist your treating physician to decide if I-PDT can be used to treat your tumor.

If your treating physician decides that your tumor can be treated with I-PDT with porfimer sodium, you will receive the following procedures:

- You will receive one dose of porfimer sodium (at 2 mg/kg of your body weight) about 48±8 hours before your scheduled experimental treatment with I-PDT. The porfimer sodium will be in a liquid that will be slowly injected into one of your veins, over 3-5 minutes.
- You will have a research blood drawn (approximately 2 teaspoons) prior to the injection of porfimer sodium.
- You will return to Roswell Park for the I-PDT treatment that will take place in the surgery room, while you are asleep.
- The physician will use the computer-based treatment plan as guidance for inserting the catheters to treat you with I-PDT. Note, the treating physician will make the final decision of how many catheters will be inserted and where they should be inserted, considering your safety and the objective to deliver an I-PDT that is most likely to be effective.
- An ultrasound system will be used, prior to catheter insertion, to confirm that the catheters can be safely placed, according to the plan. The catheters will be used to accommodate the laser fibers that will deliver the therapeutic light.
- If possible, an intraoperative CT (or other clinically approved imaging) will be used to image the catheters in the tumor.
- Laser treatment fibers with cylindrical end will be inserted into the close-end catheters. Only one laser fiber will be inserted into each catheter.
- Additionally, dosimetry (measurement) fibers to measure the laser light will be inserted into other catheters.
- The laser fibers will be connected to laser systems that will be used to deliver the therapeutic light into the tumor. In the event that the treating physician feels that there is a need to treat the superficial surface of your tumor, the treating physician will use a laser fiber (like flashlight) to illuminate the surface of your tumor. That will add approximately 6-9 minutes to the treatment.
- A light dosimetry system will be used to monitor the light during I-PDT. The laser treatment and dosimetry fibers could be moved from one catheter to another.
- At the end of I-PDT, the lasers will be turned off and all the catheters and fibers will be removed.

The effect that the treatment is having on your cancer will be closely monitored and the continuation of your treatment will be determined by how well the cancer is being controlled. The status of your tumor will be re-evaluated with physical examinations and biopsies. The status of your tumor will be re-evaluated at 6-8 weeks, 12-16 weeks and then at the discretion of your physician. You will continue to be checked every 3-12 months (physical exams and biopsies, if needed) indefinitely after you have finished the treatment as this is routine standard of care follow-up schedule after cancer treatment.

IF YOU DO RECEIVE THE EXPERIMENTAL TREATMENT, WHAT TESTS AND PROCEDURES WILL YOU HAVE DONE?

It is most likely that a single session (or course) of the I-PDT will be required to treat your tumor. However, if your treating physician believes that your tumor may require more than one course of I-PDT for complete and effective illumination, up to three sessions of I-PDT may be conducted at least 30 days apart. In each session you will receive the same dose of the drug (porfimer sodium at 2 mg/kg).

The schedule listed below will be followed in each I-PDT course.

- **Day One:** The study drug, porfimer sodium will be given through a vein in your arm, over 3-5 minutes. You will be an outpatient.
- **Because this drug will make your skin sensitive to sunlight and bright indoor light, care will be taken to shield your skin from light while you are in the clinic. You should protect yourself from sunlight for at least 30 days after the porfimer sodium is given so that the photosensitizer in your skin is not activated. Failure to protect yourself from sunlight during this time may result in a severe sunburn type of reaction (sunburn may include redness, swelling, pain and blistering in area exposed to the sun) on your skin (See Risks section for detailed information).**
- **Day Three:** You will have a research blood draw (approximately 2 teaspoons)
- The doctors will give you medicine to make you fall asleep (general anesthesia) through the entire procedure.
- We will shine a light from the laser that will cause the photosensitizer to become active and attack your cancer. The light from the laser will be transmitted through one or more laser fibers.
- During I-PDT, measurements will be taken with the dosimetry (measurement) system to record how much laser light is getting to your cancer.
- After I-PDT, the doctors will wake you up and you will be taken to another room for recovery. The doctors estimate that the entire procedure will be completed within a few hours**.**
- During your care in the clinic or hospital, the use of a pulse oximeter (this checks your oxygen level by placing a small clip onto your finger) may be used as part of normal standard care. This pulse oximeter has a small light that shines on the fingernail and could cause a small burn if it not changed every 15 minutes**.** The site used for the pulse oximeter will be changed frequently to avoid any burn.

Post I-PDT Treatment(s):

- **After receiving the porfimer sodium you must observe precautions to avoid exposure of skin and eyes to direct sunlight or bright indoor light (from examination**

lamps, including dental lamps, operating room lamps, unshaded light bulbs at close proximity, etc.) for at least 30 days. We will provide you with dark sunglasses that you should wear for at least 60 days. Some patients may remain photosensitive for up to 90 days or more. The photosensitivity (being sensitive to light) is due to residual drug, which will be present in all parts of your skin.

- Exposure of the skin to ambient (surrounding on all sides) indoor light is, however, beneficial because the remaining drug will be inactivated gradually and safely through a controlled reaction.
- You should not stay in a darkened room during this period and we encourage you to expose your skin to ambient indoor light.
- After 4 weeks, you should test your photosensitivity by exposing a small area of the skin to sunlight for one minute.
- If no reaction (that is no redness or minor burn) occurs within 24 hours, you can gradually resume normal outdoor activities, initially continuing to exercise caution and gradually allowing increase exposure to sunlight. If some photosensitivity reaction occurs with the limited skin test, you should continue precautions for another week before retesting.
- The tissue around the eyes may be more sensitive, and therefore it is not recommended that the face be used for this testing. If you travel to a different geographical area with greater sunshine, you should retest the level of photosensitivity.
- **Please note that conventional sunscreens will be of no value in protecting your skin against this type of photosensitivity.**

6. WHY WOULD YOU BE TAKEN OFF THE STUDY EARLY?

You may be taken off the study for any of the following reasons:

- Your medical condition changes.
- New information becomes known to us that would influence your decision to remain on the study.
- The treatment is no longer helpful to you. Other options for your condition will then be discussed with you.
- The sponsor of the study may decide to stop or change the study.
- You do not follow the study schedule or requirements.
- You experience unacceptable side effects.
- You no longer want to participate.

7. MUST YOU TAKE PART IN OR STAY ON THE STUDY?

Taking part in this study is voluntary. You may decide not to enter the study or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled. However, if you decide to stop being in the study, we encourage you to talk with your doctor first about such a choice, so that you are informed about any effects that might have on your health and to discuss stopping study participation.

It may be necessary to contact you at a future date regarding new information about the medication or procedures that you have received. For this reason, we ask that you notify the Patient Access office at 716-845-1049 or stop at the Registration Desk in the Lobby of Roswell Park to update us of any change in your address.

After the procedure, you may be asked questions about your experience with the investigational products and may be asked to cooperate in having laboratory tests and physical examinations your doctor considers necessary. You can refuse these requests without any penalty. Your refusal will not affect you current or future medical care and you will not forfeit any benefits for which you are entitled.

8. WHAT RISKS AND DISCOMFORTS ARE INVOLVED?

The specific risks of using the experimental devices are unknown. It is not anticipated that there will be any increased risk of using these devices over the standard PDT. However, all investigational products may involve unknown risks and unforeseen adverse reactions, including both temporary and permanent side effects. We do not yet know the side effects the use of the devices may cause. There may be unknown and unexpected side effects as a result of using these devices together.

PDT risks:

Pain

You may experience mild to severe pain for several days to weeks after I-PDT experimental treatment/surgery. The physicians will prescribe pain medications before you are discharged from the hospital.

Skin Photosensitivity

It is very important that you avoid bright light immediately after you receive the drug porfimer sodium. Porfimer sodium makes you extremely sensitive to bright lights for ***at least 30 days and for some patients (rare) this may last for up to 90 days or more.*** Bright lights include direct sunlight, bright indoor lights such as halogen or spotlights, examining lights such as those used by a dentist and intensive light such as that used in tanning salons. Exposure to direct sunlight or intense bright light will result in serious sunburn so you must take precautions to avoid exposing your skin and eyes to strong direct light.

Therefore, after receiving the porfimer sodium you must observe the following guidelines and precautions:

- Avoid exposure of skin and eyes to direct sunlight or bright indoor light (from examination lamps, including dental lamps, operating room lamps, and unshaded light bulbs at close proximity, for at least 30 days.
- You should also avoid eye examinations with bright lights for at least 30 days after the injection of porfimer sodium.
- Please note that conventional sunscreens will NOT protect your skin against this type of photosensitivity.
- You should wear dark sunglasses (that we will provide you with) for at least 60 days.
- You must wear protective clothing, including a hat, gloves, sunglasses, long sleeves and pants whenever you are outdoors in bright sunlight. This protective clothing is necessary for at least 30 days after the injection of porfimer sodium.
- At home you must draw the drapes or blinds on windows that admit bright, direct sunlight during the day.
- Some patients may remain photosensitive for up to 90 days or more. The photosensitivity (being sensitive to light) is due to residual drug, which will be present in all parts of your skin.

- You should not stay in a darkened room during this period and we encourage you to expose your skin to ambient (surrounding on all sides) indoor light.
- After 4 weeks, you should test your photosensitivity by exposing a small area of the skin to sunlight for 10 minutes. If no reaction (that is no redness or minor burn) occurs within 24 hours, you can gradually resume normal outdoor activities, initially continuing to exercise caution and gradually allowing increased exposure to sunlight. If some photosensitivity reaction occurs with the limited skin test, you should continue precautions for another week before retesting. The tissue around the eyes may be more sensitive, and therefore it is not recommended that the face be used for this testing. If you travel to a different geographical area with greater sunshine, you should retest the level of photosensitivity.

If you do not follow the precautions about avoiding strong, direct light you may suffer severe sunburn, even after exposure to sunlight for just a few minutes. This sunburn can be more severe than sunburns you may have received in the summer or in hot climates. It happens after a much shorter exposure to direct sunlight. If a photosensitivity reaction does happen to you, it will usually get better after about *10-14* days. If it is very severe, you may require treatment to reduce the swelling and discomfort. It is important to report any photosensitivity reactions to your doctor.

Some people have noticed a slight, but permanent, darkening of the skin exposed to sunlight. Photosensitivity reactions after treatment with porfimer sodium have been observed in approximately 10-15% of patients and were mostly mild, with redness and rarely mild swelling. All symptoms resolved without any lasting effect. Typically these reactions were mostly mild to moderate erythema (redness of skin) but also included swelling, itching, burning sensations, feeling hot, or blisters.

Porfimer Sodium Risks

Likely Side Effects: Those that occur in approximately 15%–30% of persons who receive this drug.

- Anemia
- Fever
- Constipation
- Nausea
- Chest pain
- Pain
- Abdominal pain
- Shortness of breath
- Photosensitivity reaction
- The formation of blisters from sunburn
- Sensitivity of eyes to bright lights
- Pneumonia
- Vomiting

Less Likely Side Effects: Those that occur in approximately 10%-14% of persons who receive this drug.

- Redness from sun exposure or from bright lights
- Unable to sleep

- Back Pain
- Sore throat
- Difficulty swallowing
- Abnormal heart rhythm
- Lungs cannot take in enough oxygen

Unlikely Side Effects: Those that occur in approximately 5%-9% of persons who receive this drug.

- Fungal infection of the mouth
- Weight loss
- Confused state
- Tumor bleeding
- Anorexia
- Esophagus swelling/irritation
- Vomiting of blood
- Low blood pressure
- Cough
- Anxiety
- Dehydration
- Urinary tract infection
- Swelling of tissues, usually in the lower limbs, due to the accumulation of fluids
- Cardiac failure
- Abnormally fast resting heart rate
- Upset stomach
- Narrowing of esophagus
- Weakness
- High blood pressure
- Chest pain
- General swelling (edema)
- Blood in stools
- Belching
- Diarrhea

Rare but Serious Side Effects: Those that occur in less than 5% of persons who receive this drug.

- Rash and itching on skin

Interstitial Photodynamic Therapy (drug and light):

During treatment, the doctor will insert metal needles into your tumor. Such a procedure is routinely used for other treatments (such as taking a tissue sample from a tumor) and has been associated with the following risks.

Likely Side Effects: Those that occur in approximately 15% - 30% of persons who undergo this procedure.

- Pain in the treated area
- Swelling in the treated area

- Bleeding within or near the tumor site after PDT

Less Likely Side Effects: Those that occur in approximately 10–14% of persons who undergo this procedure.

- Difficulty in swallowing (dysphagia)
- Transient inflammatory reactions that can be seen as fever, difficulty breathing and chest pain.
- Weight loss

Unlikely Side Effects: Those that occur in approximately 5%-9% of persons who undergo this procedure.

- General edema (swelling)
- Infection in specific areas within or near treated region
- The formation of an ulcer in the mouth

Rare but Serious Side Effects: Those that occur in less than 5% of persons who undergo this procedure.

- Bleeding within or near tumor site after PDT
- Infection in specific areas within or near treated region
- Injury to a blood vessel or another organ
- Difficulty breathing requiring tracheostomy
- There is a chance that tiny parts of the tumor (cancer cells) will be moved from their original location during the insertion and removal of the catheters.
- Death

In addition, the following complications (with no known statistics) could occur: formation of scar, formation of a pocket of clear fluid in your mouth, an opening between a salivary duct or gland and the oral cavity (oral fistula), inflammation of a salivary gland, formation of dead tissue in the mouth or skin, nerve damage, numbness.

9. REPRODUCTIVE RISKS:

This study may involve risks to you or your unborn child that are not known at this time therefore, you should not become pregnant or father a baby while you are participating in this study. Also, you should not nurse your baby while on this study. Women of childbearing potential will be required to take a pregnancy test before being allowed to take part in this study. You may also be asked to take pregnancy tests while receiving the study treatment. The pregnancy test must be negative before you enter this study.

You will be asked to practice an effective method of birth control while you are on this study and for a time after your treatment ends. This includes, but is not limited to, oral birth control pills, an IUD, condoms with spermicide, or abstinence. In women of childbearing potential, birth control should continue for six (6) months after the last treatment to ensure the drug/treatment has cleared from the body. Since interactions between the study drug and oral birth control pills cannot be ruled out, a “barrier” method of contraception (condom, diaphragm) must be used as well.

In certain cases, oral birth control pills cannot be used for birth control. Please discuss this with your doctor.

When you sign this consent form, to the best of your knowledge, you are not pregnant and do not plan to become pregnant while taking part in this study. Should you become pregnant during this study, you need to immediately tell your study doctor and obstetrician. If you wish you may request a referral for counseling or ask about counseling (such as genetic counselor, social worker, or psychologist.) to discuss this further.

Male patients must use an effective method of birth control. This can include, but is not limited to, condoms with spermicide, abstinence, or having a vasectomy. When taking part in this study, you should continue use of birth control for three months after receiving the last dose of the drug to be sure the drug has cleared from the body. Males who are receiving treatment should not donate sperm for at least three months after the study is completed. Discuss birth control measures with your doctor.

10. WHAT BENEFITS MAY YOU GET FROM THIS STUDY?

It is not known if this treatment will help you or not. If the treatment is successful, you might see a decrease in your symptoms and improvement in your quality of life. It is also possible the investigational treatments may prove to be less useful or even harmful to you. You understand that there is no guarantee that being on the study will help you. Future patients may be helped from the results and information gained from this study.

11. WHAT IF YOU DO NOT JOIN THIS STUDY?

If you do not join this study, you should discuss the options with your doctor. They may include:

1. Usual/standard treatment for your disease or condition may be appropriate. This may include treatment with other drugs, drug combinations, or possibly other research programs here or at other centers which may be testing new drugs for your type of cancer.
2. No treatment, but medications and measures to keep you comfortable. This is sometimes called supportive care.

Feel free to talk with your health care team about your disease and your treatment choices.

12. WHAT WILL THIS COST?

Examinations, scans, laboratory tests, and other medical procedures and treatments that would routinely be needed to monitor and treat your illness are known as “standard of care” services. Charges for these services will be billed to you and/or your insurance carrier in the usual manner. You will be responsible for all co-payments, deductibles, and/or account balances as determined by your individual health insurance contract.

There are many different types of insurance plans and contracts. It is not possible to tell you in advance the exact amount your insurance will pay and what your financial responsibility will be. If you wish, a financial counselor can meet with you to help answer your questions regarding insurance coverage issues before you decide to participate in this study. A Financial Counselor can be reached at 716-845-3161.

There are certain insurance plans that will not cover charges for any care related to an experimental or investigational therapy or study. These plans may deny coverage for even the

routine, standard of care medical services you will need to receive during the time you are enrolled in the study. If you have an insurance plan that does not cover participation in a clinical research study, or if you currently have no insurance coverage, a financial counselor can meet with you to provide an estimate of the costs that would be associated with participation in this study. A payment schedule can be developed if needed. A Financial Counselor can be reached at 716-845-3161.

A representative from the Patient Access Department can help you obtain authorizations from your insurance carrier when needed. A representative from the Patient Access Department can be reached at 716-845-1049.

Examinations, scans, laboratory tests and other medical procedures and treatment that are required only for the clinical research study and are not needed for the usual care of a patient with your disease are known as "research related" services. Research related services will not be charged to you or your insurance.

The following experimental procedures and devices that you will receive as part of your clinical research study are considered research related: Dosimetry System, lasers, fibers and all devices used to administer the I-PDT.

In addition, the drug porfimer sodium (Photofrin®) will be provided to you at no cost, as part of the study.

You and /or your insurance company will be responsible for charges related to the administration of drugs used in this clinical research study and for charges for medications that may be needed to prevent or control side effects.

If you develop complications or side effects from your participation in this clinical research study, medical treatment will be provided at the usual charge. A financial counselor can be reached at 716-845-3161 to provide an explanation of coverage and to answer questions you may have regarding study related billing.

13. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS STUDY?

If you believe you have been injured as a direct result of your participation in this research study, notify the Roswell Park Patient Advocate at (716) 845-1365 or the Study Doctor at (716) 716-845-4898.

Medical diagnosis and treatment for the injury will be offered, and a determination will be made regarding appropriate billing for the diagnosis and treatment of the injury. A financial counselor can be reached at 716-845-3161 to provide an explanation of coverage and to answer questions you may have regarding study related billing.

You do not give up any legal rights by signing this form. You are not prevented from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

14. WILL YOU BE PAID FOR JOINING THIS STUDY?

You will receive no payment for taking part in this study.

It is possible that this research project will result in developing treatments, devices, new drugs, or procedures. If this happens, you understand that you will not receive any financial payment from the resulting use of information gained and developed through your participation in the research study.

15. WHAT IF YOU HAVE QUESTIONS?

You are free to ask questions at any time about this study and to ask for more information from the doctor identified on this consent. If you have any questions, concerns or complaints about this study, you should contact Dr. Kimberly Wooten, MD at 716-845-2300 or 716-845-4094, at Roswell Park. In case of an emergency after regular hospital hours, you should telephone (716) 845-2300 and ask for the oncologist on call who if need to will be able to contact study primary investigator, Dr. Kimberly Wooten, MD or representative.

If you have questions about your rights as a research subject or you feel you have been injured as a result of your participation in this research study, you can call the Roswell Park Patient Advocate (Support) Office at (716) 845-1365. You should also feel free to contact the Patient Advocate Office at any time while considering participation, during participation or once your participation is complete. This office is unaffiliated with any specific research study. They can help you obtain additional information regarding your research participation and your rights as a research subject or how to proceed should you feel you have been injured as a result of your participation. They are available to discuss any problems, concerns, questions or input you may have.

Where can I find more information?

You may call the NCI's Cancer Information Service 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.

For accurate cancer information including Physician Data Query (PDQ), visit https://www.cancer.gov. PDQ is NCI's comprehensive cancer database. It contains summaries on a wide range of cancer topics; a registry of open and closed clinical trials from around the world; and a directory of professionals who provide genetic services.

16. WHAT ABOUT CONFIDENTIALITY AND USE OF PROTECTED HEALTH INFORMATION?

If you volunteer to take part in this research study, and you sign this document, you give permission to the following providers to use or disclose (release) your health information that identifies you as part of the research study described in this consent. This means that others may know or be able to find out your identity.

- Dr. Wooten and members of her research team
- Government or Regulating Agencies such as the FDA or other agencies worldwide
- Institutional Review Boards or Data Safety and Monitoring Boards at Roswell Park and its' affiliates

If you volunteer to take part in this research study, you consent to the release of your health information from other medical facilities for any moderate to life-threatening or fatal adverse events that occur while on study treatment through 30 days after treatment ends.

Study information that we may use and/or disclose can identify you in the following ways: "Protected Health Information" (PHI) can be your name; address, patient identification number; medical record number; date of birth; photographs; information about your health, including past medical history, treatment, diagnosis, test results and any other information about your health or medical condition; or about payment of charges for medical treatment found in your medical record or other records maintained by Roswell Park.

This study includes a number of researchers, businesses and government agencies. They may use your health information and share it with others. We want you to know who may use this information and how they may use it. We also want to tell you about your rights before you agree to take part in this study.

Who may use and give out information about you?

The study doctor and research staff will have this information and may give it to others during and after the study.

Who may see this information?

The study sponsor may also see this information. The "Sponsor" includes all people or companies working for or with the sponsor or owned by the sponsor. They all have the right to see this information during and after the study.

The following people, agencies and businesses may also get information about you:

- Doctors and healthcare professionals at Roswell Park
- The referring doctor
- US Food and Drug Administration (FDA)
- US Department of Health and Human Services (DHHS)
- Other federal and state agencies such as the Office of Human Research Protections, (OHRP), Office of Biotechnology Activities (OBA) and the NYS Department of Health
- National Cancer Institute (NCI)
- National Institute of Health (NIH)
- Government agencies in other countries
- Government agencies that must receive reports about certain diseases and conditions
- Institutional Review Board at Roswell Park and/or their affiliates
- Pinnacle Biologics, Chicago, IL, USA

What information may be used and shared?

Medical information that identified you and relates to your participation will be created if you take part in this study. This may include the following:

- Information from the procedures used to find out whether you are eligible to take part in this study. This may include physical examinations, blood and urine tests, x-rays and other procedures or tests, and any other information that you may release to us, including information about your health history.
- Information obtained in the course of the study including information about your response to any treatments you receive, information related to study visits and phone calls, physical examinations, blood and urine tests, x-rays and other procedures or tests, and any other information about your participation in this study.

Why will this information be used and/or shared?

The information that may identify you will be used and given out to others to carry out the research study. The sponsor will analyze (test) and evaluate the results of the study. The sponsor, its agents, government agencies, and others may visit the research site to follow how the study is being done and may review your information for this purpose.

This information may be given to the FDA. It may also be shared with other governmental agencies in this country and in other countries. This is done for participant protection and so the sponsor can receive marketing approval for any new products that may result from this research. The information may also be used to meet the reporting needs of the governmental agencies.

The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed (shared).

The information may be reviewed by the IRB at Roswell Park and its affiliates, who perform review of research as needed by law.

PHI may be used and disclosed in the creation and maintenance of a research database or repository. This information may then be used for other research, either de-identified or with further IRB review and approval. This information can be kept indefinitely.

What if I decide not to give permission to use and give out my health information?

If you refuse authorization for us to use and disclose your information as indicated above, you will not be able to be in this research study.

Your decision not to sign this authorization or to withdraw from the study will not involve any penalty or loss of benefits to which you are otherwise entitled and will not affect your access to non-research related health care here.

You may change your mind and revoke (take back) this authorization at any time, except to the extent that Roswell Park has already acted (used or disclosed PHI) based on this authorization.

What happens if I want to withdraw my authorization?

To revoke/withdraw this authorization, you must write to the study doctor (whole name is on the first page of this form) and let the doctor know that you are withdrawing your authorization to use and disclose your information. The doctor's mailing address is:

Kimberly Wooten, MD
Roswell Park Comprehensive Cancer Center,
Elm & Carlton Streets,
Buffalo, New York 14263

If you should die while enrolled in or after taking part in this study, your PHI may be used or disclosed solely for research purposes without getting any added authorization.

The results of clinical tests or therapy performed as part of the research may be included in your medical record and will not be removed from the record if you withdraw.

If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

May I review or copy the information obtained from me or created about me?

You will not have the right to review or copy aspects of your Protected Health Information (PHI) that are considered to impact the integrity (truthfulness) of this research study. At the end of this research study and at your written request, you may have access to your health information that relates to the research study. This information is kept in your medical record, which is a set of data that includes medical information or billing records used in whole or in part by your doctors or other health care providers at Roswell Park to decide about care and treatment. Access to your health information in your medical record is described in the Notice of Privacy Practices provided to you by Roswell Park. If it is necessary for your care and/or treatment, your PHI will be provided to you or your referring or primary care doctor. You will not have access to your blood, tissue, and diagnostic research study results that are performed in a laboratory/facility that is not approved to report clinical results.

If it is necessary for your care and/or treatment, your PHI will be provided to you or your referring or primary care doctor.

When does this authorization end?

This authorization does not have an end date.

What happens to my health information after it is given to others?

If you sign this form, and the information is given to other people, businesses, or government agencies, the information may no longer be protected. There is a risk that your information will be given to others without your permission.

Authorization

As a participant in this study, you allow the use of protected health information for research purposes. You understand that PHI will be used/disclosed by Roswell Park as indicated in this document. You understand that you have a right to withdraw your authorization for use of PHI in writing, but that information which has already been used or disclosed before your written withdrawal will continue to be used for research purposes. Finally, you understand PHI that has been disclosed by Roswell Park through this authorization to the study sponsor, FDA, NCI, NIH, or others may be further disclosed by them, as the PHI will no longer be protected by the federal privacy laws.

Statement of Investigator/Person Conducting the Informed Consent Discussion:

I certify that the nature and purpose, the potential benefits and possible risks associated with participation in this research study have been explained and that any questions about this information have been answered. A signed copy of this consent will be given to the participant.

SIGNATURE_____ **DATE**_____ **TIME**_____

PRINTED NAME _____

Participant's Statement of Consent:

By signing below, you agree that:

- You have been told of the reasons for this study.
- You have had the study explained to you.
- You have had all of your questions answered, including those about areas you did not understand, to your satisfaction.
- You have carefully read this consent form and will receive a copy of this form.
- You do **not** waive any **legal** rights you have under federal or state laws and regulations.
- You willingly give your consent to voluntarily join in this research study.

Participant:

SIGNATURE_____ **DATE**_____ **TIME**_____

PRINTED NAME _____

Witness Signature is needed in the following circumstances-check below:

☐ Not applicable
☐ The person consenting cannot write – mark must be made as appropriate.
☐ The person consenting cannot read - consent has been read to him/her.
☐ The person consenting cannot understand English and the consent has been verbally interpreted.
(the witness should be fluent in both English and the language of the person consenting.)

Witness Statement:

The person consenting has signed this document in my presence.

SIGNATURE_____**DATE**_____ **TIME**_____

PRINTED NAME _____

RELATIONSHIP TO PARTICIPANT_____

CONSENT HANDLING
Original to CRA-Regulatory with Race/ Ethnicity if applicable
Copy to:

- Patient
- Medical Records