H-25233- PHASE II TRIAL OF ESTROGEN RECEPTOR TARGETED TREATMENT OF NON-MUSCLE INVASIVE BLADDER CANCER WITH TAMOXIFEN

Background

Bladder cancer is a mixed group of tumors with different behaviors. Expanding the understanding of bladder cancer biology will lead to the development of new treatment plans and ultimately reducing the overall burden of the disease and treatment-related cost. Biopsies are samples of tumors that are sent to a laboratory so that tests can be done to determine the type of cancer that is present.

Tamoxifen is a drug that regulates the function of the estrogen hormones in the body .Tamoxifen is currently used in patients with breast cancer because it reduces the effect of the estrogen hormone in the growth of these tumors. New research has shown that it may also help to control bladder tumors.

The participation is voluntary, that there is no penalty or loss of benefits should a participant refuse to participate, and that participants may discontinue participation at any time without any penalty or loss of benefits. If you decide to participate, you will be one of approximately 19 participants.

Purpose

Evaluate the treatment of tamoxifen of low/intermediate-risk bladder tumors.

Procedures

The research will be conducted at the following location(s):
Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, and TMH: The Methodist Hospital.

Your participation in this study will last about 4 months.

The first study visit is called the screening visit.

After you have discussed this research study with the doctor and/or a member of his study team and if you agree to take part in this study, you will sign and date this consent form.

You will have a physical exam and you will be asked about your medical history and what drugs you are now taking.

If you are a female of child bearing potential, you will provide a urine sample to test for pregnancy. It will be documented in the Research Forms if the subject is post-menopausal or has had a hysterectomy. All subjects will be asked to use double barrier method of birth control (use two forms of birth control at the same time, such as birth control pills and condoms), including females who are not of child bearing potential.

Approximately, two teaspoons of blood will be drawn for the analysis of Complete Blood Count, platelets (a blood cell that helps blood to stop flowing from a cut) and bilirubin (is a waste product of the

normal breakdown of red blood cells).
If you have had labs drawn within two weeks prior to screening visit #1, we may be able to use those results.
A urine sample will be collected and tested for cancer cells.
Visit 2
Visit 2 will occur 1-4 weeks after the screening visit.
You will be asked about what medications you are taking. You will be given the study medication called Tamoxifen with instructions to take a single dose of 20 milligrams Tamoxifen by mouth in the evening every day for 12 weeks. Tamoxifen will start on day 1 after 1st resection of marker lesion biopsy. You will be given Tamoxifen Drug Instruction Sheet and Tamoxifen Subject Diary to record the day, date and time you take Tamoxifen.

You will undergo a cystoscopy. A small, hollow tube with a light attached at the end will be inserted through the urethra (also known as the urinary channel) so that the doctor can see inside the bladder. The tube is about as wide as a wooden pencil. The urinary channel will be anesthetized (feel numb) locally with a lubricating jelly. You will then have a bladder biopsy to remove a small piece of the tumor and some surrounding tissue. This procedure will be done in the Urology Clinic. You will usually have a small amount of blood in your urine shortly after this procedure, as well as a burning sensation with and urinary frequency (having to pass urine often) that usually lasts for 1-5 days.

The urine collected during the cystoscopy will be tested for cancer cells.

Telephone Call - 3 Days after Visit 2
You will be asked about what medications you are taking and about the days and times you took Tamoxifen.

You will be asked about how you are feeling generally and about any adverse events (changes to your body or how you are feeling since the screening visit).

Visit 3-6 weeks after last telephone call
You will be asked about what medications you are taking and be given Tamoxifen to take a single dose of 20 milligrams Tamoxifen by mouth in the evening every day for a total of 12 weeks.

You will be asked about any adverse events (changes to your body or how you are feeling since the screening visit).

Week 12- You will have another cystoscopy and bladder tumor biopsy 12 weeks after you begin taking the study medication so we can evaluate the effect of the medication.. A small, hollow tube with a light attached at the end will be inserted through the urethra (also known as the urinary channel) so that the doctor can see inside the
bladder. The tube is about as wide as a wooden pencil. The urinary channel will be anesthetized (numbed) with a lubricating jelly. You will then have a bladder biopsy to remove a small piece of

the tumor and some surrounding tissue. You will usually have a small amount of blood in your urine shortly after this procedure, as well as a burning sensation with and urinary frequency that usually lasts for 1-5 days.
The 2nd procedure will involve a resection of the remaining marker lesion (surgical removal of the remaining bladder tumor after taking Tamoxifen), and because is a larger procedure, it will happen at the Hospital as an outpatient procedure.

The urine sample collected during the cystoscopy will be tested for cancer cells.

These samples will not be banked for future use. If there is a remaining sample after the planned analyses are performed, these specimens will be kept until the completion of the study. At the end of the trial, these specimens will be destroyed in an appropriate manner.

Telephone Call - 30 Days after Visit 3 (End of Study)

You will be asked about what medications you are taking and about the days and times you took Tamoxifen.

You will be asked about how you are feeling generally and about any adverse events (changes to your body or how you are feeling since the screening visit).
.

Follow-Up Visit: 3 Months Post- 2nd Resection

1. Office Visit
2. Cystoscopy & Cytology

The following exams are done at your doctors discretion and may be requested if your doctor thinks it medically necessary.

4. History/ Physical Exam
5. Labs (Hematology, CBC/Platelets, Urinalysis, Bilirubin).

Research related health information

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, and TMH: The Methodist Hospital to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Demographic information (name, D.O.B., age, gender, race, etc.)

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, TMH: The Methodist Hospital, and NIH: NATIONAL INSTITUTES OF HEALTH and their representatives.

Agents of the U.S. Food and Drug Administration may inspect the research records including your health information. Agents of regulatory agencies such as the U.S. Department of Health and Human Services will be permitted to inspect the research records including your health information.

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, and TMH: The Methodist Hospital are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, and TMH: The Methodist Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research involves treatment. You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment. To maintain the integrity of this research study, you generally will not have access to your personal health information related to this research until the study is complete. However, your health information that is necessary to your care will be provided to you or your physician. At the conclusion of the research and at your request, you generally will have access to your health information that Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, and TMH: The Methodist Hospital maintain in a designated record set, which means 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 Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub,

and TMH: The Methodist Hospital to make decisions about individuals. Access to your health information in a designated record set is described in the Notice of Privacy Practices provided to you by representatives of the specific institution where you are being enrolled into this research study which are: Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, and TMH: The Methodist Hospital.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, NIH: NATIONAL INSTITUTES OF HEALTH and their representatives, regulatory agencies such as the U.S. Department of Health and Human Services, FDA, Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, and TMH: The Methodist Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: Guilherme Godoy, M.D.
Baylor College of Medicine Medical Center
7200 Cambridge, Suite A10.151
Houston, TX 77030

This authorization does not have an expiration date. 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.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts
Blood draw- Inserting needles into veins for collecting blood may be uncomfortable. Risks include slight bruising at the injection site, fainting, the formation of a small blood clot or swelling of the vein and surrounding tissue, bleeding from the site, and the remote possibility of infection at the site of the needle puncture. Fainting is usually harmless, of short duration, and typically produces feelings of weakness, sweating, slowing of the heart rate and an abnormal decrease in blood pressure. Care will be taken to avoid these complications.

Cystoscopy- The discomfort is nearly identical to being catheterized, which generally causes slight to moderate discomfort. There will be a feeling of fullness in the bladder and a sensation to empty during the cystoscopy examination. Infection or bladder irritation may also occur.Biopsy (removal of small amount of tissue) of the bladder requires an anesthetic (numbing jelly) and there may be some bleeding afterwards for 1-5 days. The discomfort is nearly identical to being catheterized, which generally causes slight to moderate discomfort. There will be a feeling of fullness in the bladder and a sensation to empty

during the cystoscopy examination. Infection or bladder irritation may also occur.

The risks associated with leaving a tumor in the body for study purposes are minimal as there is a low rate of progression. The Marker Lesion Trial study design consists of deliberately leaving a small visible lesion in the bladder so the patient can receive the study treatment , and shortly afterward have the lesion removed, them re-assess how effective the treatment. Marker Lesion Trial is the design of choice.The period of observation between the biopsy and the final treatment is very short and not receiving the standard mitomycin-C is considered safe.

The loss of confidentiality regarding research information is a possibility, although, the risk is low. The investigator and his staff will make every effort to maintain the confidentiality

Adverse effects of tamoxifen citrate usually are relatively mild and rarely severe enough to necessitate discontinuance of the drug in patients with breast cancer. Tamoxifen usually is well tolerated in male patients with breast cancer.

Pregnancy Warning: It is possible that the biopsy procedure could injure a fetus if you are pregnant. Because of the potential risks involved, you should not become pregnant while you are participating in this study. If you are sexually active or become sexually active and can get pregnant, females and their male partners must agree to use a double barrier method of birth control (use two forms of highly effective contraception at the same time such as birth control pills and condoms) every time you have sex between the first biopsy and the second biopsy (about 4 weeks):
oral contraceptives ("the pill"),
- intrauterine devices (IUDs),
- contraceptive implants under the skin, or contraceptive injections,
- condoms with foam.
There may be a risk of reactions to tamoxifen in nursing infants, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the woman.

There may be a risk of blood clots forming and moving within the veins or arteries such as a deep vein blood clot, stroke or a blood clot in the lung.
There may be a risk of hot flushes (flashes) and or increased hot flushes (flashes).
There may be a risk of an increase in fats or lipids in the blood while taking tamoxifen.
There may be a risk of increased fluid retention or edema.
There may be a risk of vaginal discharge and or irregular menstrual cycles, loss of libido or impotence.
There may be a risk of muscle or bone pain.
There may be a risk of vision changes.
There may be a risk of changes in your liver blood tests.
There may be a risk of nausea, changes in eating habits or abdominal cramps.
There may be a risk of feeling dizzy, have a headache, feel tired or experience depression.
There may be a risk of changes in your platelet count (a blood cell that helps blood to stop flowing from a cut)
There may be a risk hair thinning or hair loss.

There may be a risk of weight loss or a cough.
There may be a risk of cancer in the lining of the uterus or of the liver or liver abnormalities.
There may be a treatment or procedure that involve risks that are unforeseeable.

These side effects are usually temporary and do not cause permanent damage.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

Potential Benefits
You will receive no direct benefit from your participation in this study. However, your participation may help the investigators better understand The potential benefit to the subject is that tamoxifen may prevent or reduce recurrence of the disease, and also the progression to invasive stages, ultimately prolonging survival. Subjects may experience a slowing of the progression of bladder cancer and possibly improve their survival and or quality of life. The participant may receive no benefit..

Alternatives
You may choose to not participate in this study.

Subject Withdrawal from a Study

If you decide to stop taking part in the study or if you are removed from the study, you may decide that you no longer allow protected health information that identifies you to be used in this research study. Contact the study staff to tell them of this decision, and they will give you an address so that you can inform the investigator in writing. The investigator will honor your decision.

Investigator Withdrawal of Subject from a Study

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you do not take your study medication, or if you have a serious reaction to your study medication) or because the entire study is stopped. The sponsor, investigator, Food and Drug Administration, or Institutional Review Board may stop the study at any time.

Subject Costs and Payments

You will not be asked to pay any costs related to this research.

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

Research Related Injury

It is important that you tell your study doctor, Guilherme Godoy, if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him at 713-798-4001.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

In the event of injury resulting from this research, Baylor College of Medicine and/or the Harris Health System not able to offer financial compensation or to absorb the costs of medical treatment. However, necessary facilities, emergency treatment and professional services will be available to you, just as they are to the general community."

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Women of Childbearing Potential

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study.

If you are sexually active or become sexually active and can get pregnant or can get your partner pregnant, you must agree to use one of the following forms of birth control every time you have sex:

* oral contraceptives ("the pill"),
* intrauterine devices (IUDs),
* contraceptive implants under the skin, or contraceptive injections,
* condoms with foam.

The Investigator will discuss the risks and benefits of each of the different forms of contraception available to you in an effort to provide you with the information necessary for you to make a fully informed decision as to which form of contraception you will use.

There is specific information available about the risks of each form of contraception and there is also information available about the "failure rates" of each form.

Should you become pregnant while on this study, you must immediately notify the study personnel.

The investigator will assist you in finding appropriate medical care. The investigator also may ask to be allowed to continue getting information about your pregnancy. You can choose not to provide this information.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

The investigator, GUILHERME GODOY, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: GUILHERME GODOY at 713-798-7303 during the day and after hours.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date