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UNIVERSITY OF WASHINGTON
Fred Hutchinson Cancer Research Center
Seattle Cancer Care Alliance

Consent to take part in a research study:

Acupuncture vs. Standard of Care for Induction Intravesical BCG-Related Adverse
Events in High-Risk Non-Muscle Invasive Bladder Cancer

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Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to understand whether or not acupuncture can be helpful in reducing the side effects of intravesical *Bacillus Calmette-Guerin* (BCG) therapy in patients with high risk, non-muscle invasive bladder cancer. People who agree to join the study will be randomized to receive standard of care symptom management or standard of care symptom management plus the acupuncture intervention, as described in this consent form. All participants will be asked to fill out follow-up questionnaires over the planned six cycles of induction intravesical BCG. Acupuncture is a traditional Chinese medical treatment which involves the use of very small, thin needles to stimulate specific points in the body. Previous studies have found a benefit of acupuncture for the treatment of over active bladder (OAB). This study will test whether acupuncture can decrease the symptoms akin to OAB secondary to intravesical BCG instillations for high-risk bladder cancer.

We are doing this research study to answer these questions:

1. Is it feasible for patients to undergo acupuncture therapy prior to receiving intravesical BCG?
2. Does acupuncture therapy, performed prior to intravesical BCG instillation, result in decreased side effects of the BCG treatment?
3. Is there a difference in health-related quality of life between patients who do and do not receive weekly acupuncture prior to intravesical BCG therapy?
4. Does acupuncture therapy result in reduced need for other medications to manage side effects of BCG intravesical therapy?
5. Does acupuncture prior to intravesical BCG result in a decrease in missed BCG doses or need for dose reduction among patients receiving intravesical BCG for bladder cancer?

We would like you to join this research study.

We are doing this study to understand if adding a weekly acupuncture therapy session prior to 6 weekly intravesical BCG instillations will benefit patients with high risk non-muscle invasive bladder cancer. We want to learn how we can help patients who need BCG therapy tolerate this medication better, with fewer side effects, to both improve the ability to complete the full regimen of BCG, and also to improve their quality of life while they are going through therapy. Since you have been diagnosed with high risk non-muscle invasive bladder cancer with no evidence of metastatic disease and have decided with your physician to undergo six weeks of induction intravesical BCG therapy, and are older than 18 years of age, we would like to ask you to join this research study. We will enroll up to 45 people.

You do not have to be in this study. You are free to say yes or no, or to drop out after joining. There is no penalty or loss of benefits if you say no. Whatever you decide, your regular medical care will not change.

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Below is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

What research tests and procedures are part of this study? / What will happen in this study?

If you decide to join this study, we will do these tests and procedures:

Baseline Study Visit: Your first study visit will take place at the University of Washington Medical Center (UWMC) in the Urology clinic. Before any data collection, the study investigators will explain the study activities, rights and responsibilities to you. *After signing the informed consent form, you will undergo:*

1. An interview to collect information on your demographics (age, gender, ethnicity, etc.), medical history, health and functional status,.

We will also give you a medical records release form for permission to collect medical records relating to your cancer diagnosis and treatment from your doctor.

We will give you a study package with information and materials needed to participate.

Randomization: After completing the data collection mentioned above, you will be randomized (sorted) to one of two study groups. Regardless of which group you are randomized to, you will be asked to arrive at the UWMC Urology Clinic 1 hour prior to your scheduled weekly BCG instillation. After you arrive and are checked in, you will give a urine sample to ensure you do not have any blood in your urine or evidence of a urinary tract infection. You will then be escorted to a quiet room.

1. **Acupuncture plus Standard of Care Group:** If you are randomized to participate in the acupuncture group, you will have an acupuncture therapy session prior to each BCG instillation procedure which will take approximately 30-45 minutes. Following the session, you will be brought into the clinic procedure room and will undergo BCG instillation per the standard protocol that your physician explained to you.
2. **Standard of Care Group:** If you are randomized to participating in the standard of care arm, you will be invited to relax while you wait for your appointment time, and then will be brought into the clinic procedure room where you will undergo BCG instillation per the standard protocol that your physician explained to you. At the conclusion of the study, you will be given coupons to receive 4 free acupuncture appointments.

Regardless of which arm you are randomized to; you will receive the same medication following treatment for any possible symptoms related to the BCG instillation and will also receive the same instructions regarding management of your symptoms.

Study staff will contact you over the phone to inform you of your group assignment. Following the phone conversation, we will mail you a study package that will include a study activities schedule.

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Study Measurements:

Questionnaires: While you wait for your treatments each week, you will be asked to two questionnaires regarding your overall quality of life (EORTC-QLQ-C30) and your quality of life specific to the diagnosis of bladder cancer (EORTC-QLQ-NMIBC24) and a journal regarding your medication and dietary supplement use for the prior week. Before you receive your first dose of induction BCG, we will provide you with these questionnaires through email, phone, or mail according to your preference. There will be 4 questionnaires included in this first packet, which includes 15-50 questions in each. The study questions will take approximately 30-35 minutes for you to fill out.

Health Care Use for Bladder Symptoms while on BCG: We will keep track of any extra visits to the clinic, the ER, or your other doctors that you require during these six weeks for management of your bladder cancer symptoms.

Length of time BCG is able to be retained in the Bladder: Following instillation of your BCG, we will reach out to you via text/email to ask you when you emptied your bladder. This will allow us to record how long you were able to hold the BCG in your bladder.

How long will I be in this study?

You will be in this study for **approximately 8 weeks**, including one week prior to starting BCG, the six weeks for the induction course of BCG one additional week for follow-up. Should you need to miss a week of BCG therapy, the study will continue as long as you are receiving induction BCG. If you stop BCG therapy early, you will also complete the study early. We will also keep track of any negative side effects or complications of the BCG therapy.

The principal investigator for this study or your doctor may take you out of this study at any time. This would happen if:

- They think it is in your best interest to stop participating in the study.
- You are unable or unwilling to follow study procedures.
- The whole study is stopped.

If you are thinking about not continuing with this study, please tell us. We will talk to you about any other follow-up or testing that would help you.

If you leave the study, your test results and information cannot be removed from the study records.

Risks of being in this study

There are some potential risks to participating in this study. These potential risks are listed below. There may be some unknown risks linked with being in this study that are not listed.

Study Questionnaires: You may feel uncomfortable, embarrassed, or self-conscious about answering the study questionnaires. These questionnaires are validated tools which have been designed for patients with bladder cancer to describe urinary symptoms related to their bladder cancer, the therapies they are receiving, and their overall quality of life. You do not have to answer any part of the questionnaires or other assessments; you may ask to skip questions that may make you feel uncomfortable. Study staff will also discuss how information will be kept confidential.

Loss of confidentiality: A risk of taking part in this study is the possibility of a loss of confidentiality. Loss of confidentiality means that your personal information could be shared with someone who is not on the study team who was not supposed to see your information. We will try to protect your information, but we cannot guarantee privacy. The plans for keeping your information private are described in the 'confidentiality' section of this consent form.

Physical injury: Research related injuries are unlikely due to the low risk nature of this study; however, there is a risk of unintentional injuries that may occur during the acupuncture therapy sessions if you are randomized to the acupuncture arm. There is a minor risk of bruising, bleeding, pain at the acupuncture needle insertion site, redness, or allergic reaction. There is a very rare chance of fainting, infection, or organ puncture.

Inconvenience: The visits for your BCG instillations may be slightly longer due to the need for the acupuncture therapy/waiting for your treatments, as well as the time required to fill out the weekly questionnaires. It is also possible that we may need to contact you regarding your questionnaires outside of your standard visits, which could potentially cause you inconvenience.

Other risks: There may be other risks of taking part in this research study that we don't know about. If we learn about other risks, we will let you know what they are so that you can decide whether or not you want to continue to be in the study.

What are the benefits?

We do not know if this study will benefit participants. We hope that the information we learn will help patients with bladder cancer undergoing induction BCG in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say yes or no. Your regular medical care will not change. Enrollment in this study may exclude you from other research studies.

Your other choices may include:

- Following your physician's or treatment team's directions for medications and other strategies to manage potential symptoms and adverse effects of intravesical BCG therapy.

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- Other research studies.

Protecting your Privacy as an Individual and the Confidentiality of Your Personal Information

Some people or organizations may need to look at your research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect your rights as a research participant.
- Fred Hutchinson Cancer Research Center, University of Washington, Seattle Cancer Alliance.
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections and other agencies as required.

We will do our best to keep the personal information in your medical record confidential. But we cannot guarantee total confidentiality. Your personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use your personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

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.

This research is covered by a Certificate of Confidentiality from the U.S. government. This Certificate helps protect the confidentiality of information about people who join this study. If you join the study, the Certificate means that generally we would not have to give out identifying information about you even if we were asked to by a court of law. We would use the Certificate to resist any demands for identifying information.

We could not use the Certificate to withhold research information if you give written consent to give it to an insurer, employer, or other person.

This protection has some limits. We would voluntarily provide the information:

- To a member of the federal government who needs it in order to audit or evaluate the research.
- To the funding agency and groups involved in the research, if they need the information to make sure the research is being done correctly.
- To the federal Food and Drug Administration (FDA), if required by

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- To someone who is accused of a crime, if he or she believes that our research records could be used for defense.
- To authorities, if we learn of child abuse, elder abuse, or if participants might harm themselves or others.

Will you pay me to be in this study?

If you complete this study, and are randomized to the acupuncture arm, you will receive all acupuncture treatments for free as a part of the protocol. If you are randomized to the standard of care (no acupuncture) study arm, you will receive coupons for 4 acupuncture sessions that you may schedule at your convenience following the conclusion of the study. If you are in the control arm and drop out of the study, you will not be eligible to receive the coupons for free acupuncture.

How much will this study cost me?

There may be some extra costs for being in the study. These costs may include loss of time spent working should your visits for BCG therapy be longer than usual, however, the study is designed to be carried out in the time you would normally be asked to set aside for BCG intravesical therapy.

What if you get sick or hurt after you join this study?

For a life-threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact the Principal Investigator Dr. Sarah Psutka, at the UWMC Urology clinic (Phone: 206-598-4294). She will treat you or refer you for treatment as appropriate. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

What will my information be used for?

Your information will be used for the purposes of this study. Your information, including medical records relating to your cancer diagnosis and treatment, and questionnaires you complete for this study, will be used to understand how well the study activities (e.g. the acupuncture therapy) function to help people tolerate intravesicle BCG.

In addition, be aware that by agreeing to participate in this study, your information could be used for future research studies or sent to other investigators for future research studies.

without additional consent from you. These future research studies will be reviewed by an oversight group known as an institutional review board (IRB) if required by law. The information that identifies you will first be removed from your information.

Your rights

- You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.
- If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you change your mind about being in this study. If we learn these kinds of information, we will tell you.

For more information

If you have questions or concerns about this study, you can talk to your doctor anytime. Other people you can talk to are listed below.

If you have questions about:	Call:
This study (including complaints and requests for information)	206-598-4292 (Dr. Sarah Psutka) 206-667-4502 (Dr. Heather Greenlee) 206-598-0061 (Samia Janat MPH, Project Coordinator)
If you get sick or hurt in this study	206-598-4292 (Dr. Sarah Psutka)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Research Center)

Signature

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent;
and
- agree to participate in this study.

Participant (age 18+)

Printed Name

Signature

Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

Printed Name

Signature

Date