McGuire Institutional Review Board
Consent Form

Template Version Date: 1/29/2019

Title of Research Study: Phase 1 Dose-Frequency Escalation Study of Neoadjuvant Cryotherapy in Locally Advanced Esophageal Cancer

Sponsor: Investigator Initiated

Protocol No.: SHAH 008

Investigator Name & Address: Joseph Spataro, MD, Dept. of GI/Hepatology (111N), McGuire VA Medical Center, 1201 Broad Rock Blvd, Richmond, VA 23249

Key Information:
This initial information is being provided to help you decide whether to participate in this study. This purpose of this study is to determine the safety, effectiveness, and tolerability of repeated spray cryotherapy (freezing) procedures on the tumors of people who have been diagnosed with esophageal cancer. Your participation in this study will last up to 13 weeks, and will require 2-3 spray cryotherapy sessions, which will be done during EGD (upper endoscopy) procedures during this time. After you read the consent, you may decide that you do not want to participate.

You may choose to participate in this study because the spray cryotherapy procedure may help treat your tumor and improve associated symptoms. You may choose not to participate because of the risk of side effects of this procedure.

Additional detailed information is provided for your review in the sections below. Ask the research team questions until you feel you have enough information to make your decision to participate or not. Participating in this research study is completely voluntary. Your decision to participate or not will have no effect on any of the services, benefits or rights that you are otherwise entitled.

The person in charge of this study is Dr. Joseph Spataro, and his contact information is listed below. If you have any questions, concerns or complaints about your rights as a research subject you may contact the **McGuire Institutional Review Board (IRB) at (804) 675-5676.** The IRB is responsible for reviewing research in humans and making sure that their safety and rights are protected.

1. Whom should I contact for questions?
If you have any questions, concerns or complaints regarding this study, unexpected reactions, or you are injured and become ill as a result of participation in this study please call AM or PM*:*

	Office	Off Hours
Dr. Spataro	**(804) 675-5021**	**(804) 675-5021**
Study Coordinator	**(804) 675-6924 or (804) 675-6789**	

If you are unable to reach any of the study staff listed and need immediate medical assistance, please call the VAMC hospital operator at 800-784-8381 and ask for the Emergency Room physician to obtain advice, or call the **Emergency Room directly at (804)-675-5527**.

2. What is this research study about?
You are being asked to participate in this research study because you have been diagnosed with esophageal cancer, and are already scheduled to undergo chemotherapy and radiation treatments. The main purpose of this study is to determine the safety and tolerability of a procedure called Liquid Nitrogen Spray Cryotherapy (LNSC or spray cryotherapy). A series of spray cryotherapy procedures (using liquid nitrogen to freeze the tumor in your esophagus) will be performed to determine whether these procedures will help treat the tumor, and whether cryotherapy will improve your quality of life and ability to swallow.

The device used to deliver the cryotherapy in this study has been approved by the US Food and Drug Administration (FDA).

The spray cryotherapy procedure will be done during a series of upper endoscopy (EGD) procedures. EGD is a procedure where a flexible lighted tube (endoscope) is passed into your esophagus, stomach and duodenum (first part of your small intestine). This allows your doctor to see inside these organs.

A total of up to 18 people will take part in this study. Your participation in the study will last up to 13 weeks.

Dr. Joseph Spataro is conducting this study at McGuire VA Medical Center and Virginia Commonwealth University (VCU).

3. What is expected of me?
If you agree to participate, you will be asked to sign this consent form before any study procedures are done.

- The study doctor will review your medical and surgical history and ask questions to make sure you are eligible to participate.
- You will be asked to complete a questionnaire about your difficulty swallowing and your quality of life. This will take about 10 minutes to complete.
- If you are a woman capable of having a child, urine will be collected for pregnancy testing. If the test shows that you are pregnant, you will not be able to participate in the study.

The timing at which you enter the study will determine the number of cryotherapy treatments you will be assigned to receive as part of this study. You will be assigned to one of the following groups:

Group 1: Two spray cryotherapy treatments at Baseline, Week 2
Group 2: Three spray cryotherapy treatments at Baseline, Week 2, Week 4

EGD is routinely done to evaluate the severity of cancer of the esophagus (your swallowing tube) and for the administration of the spray cryotherapy. Baseline and Week 2 EGD procedures are done as part of routine clinical care. The EGD and cryotherapy procedures at Week 4 (if you are assigned to Group 2) are being done only for the purposes of this research study.

Treatment

- During the upper endoscopy procedure, the study staff will perform the spray cryotherapy (freezing of tissue in your esophagus). A routine part of the cryotherapy procedure is the insertion of a decompression (suction) tube, which keeps the liquid nitrogen from collecting in your stomach.
- Applications of the freezing spray typically take less than 15 minutes.
- Biopsies (tissue samples from your esophagus) are routinely taken as part of the upper endoscopy procedure. A small amount of the tissue will be examined for research purposes related to this study.
- After the procedure, you will be observed for at least 30 minutes.
- A blood sample will be collected for testing before the first and second spray cryotherapy procedure, and then again at the end of your chemotherapy/radiation therapy treatment.
- If you are a female who can become pregnant, a urine pregnancy test will be done at least monthly while you are participating in the study.
- You will be given standard post-endoscopy instructions which include: clear liquids only for 24 hours, and then avoiding hard, crunchy foods for a week. You will be asked not to use medications such as blood thinners and certain anti-inflammatory drugs, unless instructed otherwise by your doctor.

Unscheduled Study Visits
The study doctor may ask you to return for an unscheduled study visit if your condition worsens or if the study doctor thinks that you need to be evaluated.

Phone Calls/Medical Record Review
The study staff will contact you by telephone at 48 hours and at 1 week following each spray cryotherapy treatment to ask you questions about your swallowing, ability to eat, any side effects, and how you are feeling. It will take about 10 minutes to answer these questions.

In between study clinic visits, the study staff will be reviewing your medical records to monitor any changes in your health or any hospitalizations.

4. Future Use of Data/Samples Collected During the Study
Identifiers might be removed from the identifiable private information and/or identifiable biospecimens that are collected. After that removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional consent from you.

Dr. Spataro asks that you allow him to keep a portion of your biopsy specimens collected during the study to be used for future testing. If you agree to this, a portion of your samples will be stored in a research laboratory at the McGuire VA Medical Center. Your samples will be de-identified. This means that a code, but no information that identifies you, like your name or your birthday, will appear on the samples. You do not have to agree to this to participate in the study. If at any time during or after the study, you decide that you want your samples destroyed, you can contact Dr. Spataro at 804-675-5021 and your samples will be destroyed.

I agree to allow Dr. Spataro to keep a portion of my specimens collected during the study for future testing. Please check one:

YES ☐ ___Initials

NO ☐ ___Initials

5. Will the research benefit me?
You may or may not benefit from participating in this study. Information obtained from this study may help subjects with esophageal cancer in the future.

6. What are my alternatives to being a research subject?

You do not have to participate in this study to receive treatment for your condition. The study doctor will discuss other available treatments with you. You may decide not to participate in this study or have no treatment.

7. What are my risks?
You may experience one or more of the side effects listed below. Some of these side effects may be severe and can result in death.

EGD Risks
Common side effects and discomforts associated with EGD with cryotherapy include:

- Gagging
- Nausea
- Vomiting
- Bleeding
- Sore throat
- Difficulty swallowing

The most common side effect/discomfort following EGD with cryotherapy is mild chest pain which usually goes away after 24-72 hours.

There is a rare risk that the endoscope may perforate (make a hole) in the esophagus or stomach, requiring surgery to repair.

There is a rare risk of bleeding requiring treatment, such as blood transfusion, repeat EGD or surgery.

Risks of EGD are not limited to the above. The study doctor will explain them to you in more detail and you will be asked to sign a separate consent form for EGD before the procedure is performed. EGD with cryotherapy will take about 30 minutes to complete.

Sedation
You may receive sedative medications during the EGD procedure. Any drug used for sedation may cause drowsiness, slow your breathing, and lower your blood pressure. You will be monitored closely during the procedure in case you experience any of these side effects.

All drugs have the potential to cause allergic reactions. Allergic reactions may be mild to severe, and include the following symptoms: chills, fever, skin rash, hives, itching, watery eyes, swelling, headache, difficulty breathing, difficulty swallowing, severely low blood pressure, organ failure, and death. Serious allergic reactions require immediate medical attention.

Blood Draws
The risks of blood drawing include pain, bleeding, and bruising. You may experience dizziness, nausea or fainting during blood draw. Rarely, a small blood clot or infection may occur at the site of the needle puncture.

Unforeseen Risks
Participation in this study may involve risks that are unknown at this time. Your condition may stay the same, may improve or may worsen from study participation.

Esophageal cancer is a serious disease with many possible complications whether or not you participate in this study.

8. Will I get paid?
You will not be paid for study participation.

9. Will I have to pay?
You will not have to pay for care received as a subject in a VA research project regardless of whether you are a Veteran or a non-Veteran. If you get a bill for research services, contact your study doctor or research nurse. Some Veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services provided by the VA that are not part of the study.

All tests and procedures required for the study that are not part of your regular medical care will be provided to you at no cost.

10. Does pregnancy prevent me from participating?
Every effort will be made to have females enter this study, but pregnant women will not be enrolled. Women who can become pregnant must agree to use a reliable method of birth control throughout this study. If you suspect you have become pregnant, you must let the study doctor know immediately – do not wait until your next appointment.

Reliable methods include:
- Abstinence - not having sexual intercourse
- Hormonal contraception (for example, birth control pills, patch, implant)
- IUD (intrauterine device)
- Partner who has had a vasectomy

No birth control method completely eliminates the risk of pregnancy. If you are a female and if pregnancy occurs there may be a risk of miscarriage, birth defects, other medical complications or unknown risks to yourself or to the unborn baby. If you are a female of childbearing age, you must have a negative pregnancy test before entering the study.

11. What if I get injured?

In the event of injury resulting from your participation in this research study, McGuire VA Medical Center may or may not provide compensation, depending on applicable federal regulations. A research injury is any injury or illness directly caused by your participation in the study. In the event of a research injury, necessary medical treatment will be provided to assist your recovery from the injury. For research-related injury, the VA must provide necessary medical treatment regardless of whether you are a Veteran or a non-Veteran.

This agreement to provide medical treatment does not include treatment for injury or illness that is not a direct result of the study. A study-related injury does not include injuries directly caused by any of the following: the natural course of your underlying disease or medical condition, or not following the instructions provided in this consent form or by study staff. You are not giving up any of your legal rights by signing this form.

12. Who Will See My Information?

The confidentiality of your research records will be maintained according to professional standards of confidentiality and VA regulations. Records identifying you may be reviewed by the members of the research team, the Research and Development Committee and its sub-committees, accrediting agencies, officials from the Veterans Health Administration, the Office of Research Oversight, the VA Office of the Inspector General, Richmond VAMC, and other federal oversight agencies such as the Office for Human Research Protections, or as required by law.

The information collected about you while you are in the study such as your name, age and social security number will be protected. For example, only Dr. Spataro and his study staff will have access to your study records which will be kept in locked filing cabinets and on computers protected with passwords.

The ways your study doctor will use your study-related health information and the people who may receive it are identified in a separate form entitled, Authorization for Use & Release of Individual Identifiable Health Information for Veterans Health Administration Research. You will be asked to sign that form to show that you give permission for these uses and sharing of your information. You do not have to sign the authorization form. However, if you do not sign, you will not be able to participate in the study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Information published or presented about the results of this study will not identify you.

13. Do I have to participate in this study, or can I withdraw from the study?
Participation in this study is voluntary and you may refuse to participate without penalty or loss of benefits to which you are otherwise entitled. The study staff will answer any questions you may have about the study. You are free to withdraw your consent and stop participation at any time. If you decide to withdraw from this study, you should contact Dr. Spataro to discuss termination of your participation. Stopping will in no way change the quality of care you receive now or in the future at this institution or your right to participate in other studies.

Any significant new findings that develop during the research study that may affect your decision to continue participating will be provided to you as soon as possible.

Your participation in this research study may be ended without your consent for the following reasons:

- If the study doctor believes, for any reason, that it is within your best interest
- If you develop side effects that are considered dangerous
- If you are pregnant
- If other causes prevent continuation of the clinical research study
- McGuire IRB may also end the study at any time.

14. Date of Consent Form Revision: December 20, 2019; May 25, 2021; May 19, 2022; July 11, 2022

Subject Name:_____ **Date:**_____

Research Study Title: Phase 1 Dose-Frequency Escalation Study of Neoadjuvant Cryotherapy in Locally Advanced Esophageal Cancer

Principal Investigator*:* Joseph Spataro, MD **VAMC:** Richmond

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above.

Dr. Spataro (or an associate) has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled. The results of this study may be published, but my records will not be revealed unless required by law. By signing below, I am agreeing to participate in this research study. I will receive a signed copy of this consent form.

_____ _____

Subject's Signature **Date**

_____ _____

Signature of Person Obtaining Informed Consent **Date**