Official Title: Cryocompression for Bortezomib-Induced Peripheral Neuropathy Among Multiple Myeloma Patients
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Wake Forest®
School of Medicine

Department/Section of *Internal Medicine/Hematology & Oncology*

CYROCOMPRESSION FOR BORTEZOMIB-INDUCED PERIPHERAL NEUROPATHY AMONG MULTIPLE MYELOMA PATIENTS

Informed Consent Form to Participate in Research
Roy Strowd, MD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to evaluate the feasibility of daily 30-minute cryocompression treatments in multiple myeloma patients with neuropathy (nerve pain or tingling in hands or feet). You are invited to be in this study because you are currently experiencing symptoms of neuropathy from your multiple myeloma treatment. Your participation in this research will involve five study visits and daily 30-minute cryocompression treatments for 8-weeks. Cryocompression is a treatment where you wear a glove and a boot that cools down your skin. Your total time in the study will be about 8-10 weeks.

Participation in this study will involve various medical tests, questionnaires, and cryocompression treatments. All research studies involve some risks. These risks may include some discomfort or pain from study procedures. There is the possibility that your neuropathy symptoms may improve and you could benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include medications to treat neuropathy, creams to reduce pain, or not participating in the study. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Roy Strowd, MD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information is: [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are experiencing symptoms of neuropathy (pain or tingling in your hands or feet) from your multiple myeloma treatment. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to see if patients with multiple myeloma can undergo a treatment called cryocompression to treat neuropathy caused by a medication called bortezomib. Cryocompression is a treatment where patients wear a glove and a boot that cools the skin. This cooling treatment is safe and has helped reduce other types of pain. Peripheral neuropathy (nerve pain or tingling in your hands or feet) is a common side effect of chemotherapy that affects the quality of life and amount of chemotherapy that can be given to many cancer patients. Bortezomib is a medication used to treat multiple myeloma and often causes peripheral neuropathy. Cryocompression has helped reduce pain in post-operative patients who have undergone a surgery. Cryocompression is safe and does not interfere with chemotherapy treatment. In this study, you will use the VascuTherm cryocompression device that has been FDA approved for treating problems like swelling in the leg and pain after surgery or traumatic injuries. We are investigating if multiple myeloma patients will be able to tolerate daily cryocompression to help reduce neuropathy caused by bortezomib chemotherapy.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

24 people here at Wake Forest Baptist Medical Center will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

At your first study visit, you will receive a physical exam of your nerve sensation and your medical history will be reviewed. If you are still eligible for our study, you will be asked to complete a questionnaire about your neuropathy pain. You will also be scheduled for your next study visit that will take place in approximately 1-2 weeks.

At your second visit, you will receive a standard evaluation of your neuropathy. This will take place at the Wake Forest Baptist Health Diagnostic Neurology Clinic. This will involve a nerve conduction test, ultrasound imaging, and blood draw. These are standard ways to see how your nerves are doing. This will last approximately 2-2.5 hours.

Your third study visit is the treatment initiation visit. This will take place at the Wake Forest Baptist Health Comprehensive Cancer Center, 3rd floor. At this visit, you will receive your first cryocompression treatment in the clinic. We will monitor your skin temperature before and after the treatment. You will also undergo ultrasound imaging before and after your initial

cryocompression treatment. After this visit, a staff member will arrange for you to begin treatments at home. A representative will come to your home to help you set up the home device and explain how everything works. This will take 45-60 minutes.

You will then complete home cryocompression treatment on your non-dominant hand and foot for 30 minutes each day for 8 weeks. You will be expected to keep a daily treatment log during this 8-week period. Unilateral treatment, or treating only the non-dominant hand and foot, allows for the comparison of neuropathy symptoms between the side of your body receiving treatment (non-dominant) and the side of the body not receiving treatment (dominant).

You will be seen in clinic every 4 weeks during treatment. This will take place at the Wake Forest Baptist Health Comprehensive Cancer Center, 3rd floor. After 8 weeks, your treatment will stop and you will be seen in clinic. During this visit you will complete the same questionnaires you completed at the beginning of the study. A physical examination will be performed and you will undergo the same neuropathy assessment completed prior to the study at Wake Forest Baptist Health Diagnostic Neurology Clinic. This will involve a nerve conduction test, ultrasound imaging, and blood draw. This will last approximately 2-2.5 hours. You will also complete a cryocompression treatment at the Wake Forest Baptist Health Comprehensive Cancer Center, 3rd floor with monitoring of your skin temperature and ultrasound imaging before and after treatment.

At the end of the study, you will be responsible for returning the home cryocompression device, and all device accessories as well as all other study-related items.

During this study, a total of 4 tubes (approximately 24 mL) of blood will be collected during the study. Two tubes (12 mL) will be collected at the beginning and two tubes (12 mL) will be collected at the end of the study.

Test results will be available in your medical record.

Identifiers (your name, address, date of birth, etc.) might be removed from the private information or blood samples that were collected as part of this research. When the identifying information is removed, your private information or blood samples may be used for future research studies or given to other research investigators without getting additional informed consent from you.

Storage of Biological Samples

If you agree to participate in this study, we will store the two tubes of blood collected from your two study visits to use for future research. This sample will be kept and may be used in future research to learn more about other diseases. Your sample will be obtained from a phlebotomy lab at Wake Forest University Baptist Medical Center. Your samples will be stored and will be given only to researchers approved by Roy Strowd, MD. An Institutional Review Board (IRB) must also approve any future research study using your blood sample. In order to participate in this study, you must be willing to provide this sample for future research.

Your blood sample will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

The research that may be performed with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood sample will not affect your care. Your blood sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of this research.

Sometimes blood samples used for genetic research may provide information about diseases that are passed on in families. Even if your blood sample is used for this kind of research, the results will not be told to you or members of your family and will not be put in your health records.

The choice to let your blood sample be kept for future use is up to you. No matter what you decide to do, it will not affect your care in this study. If you decide now that your blood sample can be kept for research, you can change your mind at any time. Just contact your study investigator, ***Roy Strowd, MD*** *at* [redacted] and let him know that you do not want your blood sample used and it will no longer be used for research. Otherwise, the blood sample may be kept until it is used up or it is destroyed.

____YES you many contact for future research studies
____NO I do not want to be contacted regarding future research studies.

____YES I do want to participate in the storage of blood sample portion of this study.
____NO I do not want to participate in the storage of blood sample portion of this study.

How Long Will I Be in the Study?

You will be in the study for about 8-10 weeks.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff right away. There are no health or safety consequences if you withdraw.

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WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the nerve conduction, ultrasound, blood draw, and cryocompression therapy we are studying include:

Nerve conduction is a standard procedure performed for patients with peripheral neuropathy. This may include some discomfort or pain from the procedure. Nerve conduction studies are one way to determine how well your nerves are sending signals. You will have 2 electrodes stuck on the skin (like Band-Aids) along a nerve and the nerve will be stimulated with a mild, brief electric shock. This will be done twice and is a part of the normal care to assess neuropathy.

Ultrasound is a safe procedure. You may experience a slight warming and/or coldness from the gel. Standard precautions will be used for these tests. The risks are not expected to be different from routine clinical procedures. This procedure will be done to look at the size of your nerves. It is done as part of the workup for nerve problems. A small amount of jelly will be placed on your skin over a nerve. The ultrasound will then slide along your skin using high frequency sound waves to look at your nerves. Ultrasound is also used to look at babies when they are growing inside their mother. This test is safe and is not painful. This will be done four times and is a part of the normal care to assess neuropathy.

All of these studies are considered standard clinical tests for the evaluation of peripheral neuropathy. The nerve conduction and ultrasound will take about 30 minutes total to complete.

You may experience skin irritation, feeling that skin is cool or cold, or mild pain or discomfort at the site of cryocompression treatment. We do not expect any long-term, or life-threatening risks.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

The principal investigator (Roy Strowd, MD) will be assisted by other members of the research team in reviewing the data and safety from this research throughout the study.

For blood draws, you may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy, lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: improvements in your neuropathy.

Based on experience with cryocompression in other research studies involving patients with post-operative pain, chronic pain, and patients with neuropathy from chemotherapy, researchers believe cryocompression may be of benefit to participants with your condition. Because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:

Medications
Topical creams
Observations

Your neuropathy may improve, stay the same, or get worse with any of these options.

WHAT ARE THE COSTS?

All study costs, including cryocompression therapy and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

- Cryocompression device provided by TruTech Medical:
  Neither you nor your insurance company will be billed for the investigational device.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

WILL YOU BE PAID FOR PARTICIPATING?

You will be provided with parking passes for all study visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest Baptist Comprehensive Cancer Center and TruTech Medical. The sponsor is providing medical devices to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call *Roy Strowd, MD* at [redacted] or the *Wake Forest Baptist Comprehensive Cancer Center* at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes: age, body-mass index (BMI), multiple myeloma staging, types and dosages of chemotherapy received, pain medications, and other medical conditions.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from TruTech Medical; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Roy Strowd, MD you want to take away your permission to use and share your

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Protected Health Information at any time by sending a letter to this address:

Roy Strowd, MD

[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

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 Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or

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safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be for your best medical interest, your condition has worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, *Roy Strowd, MD* at [redacted]. After hours you can call the *Wake Forest Baptist Comprehensive Cancer Center* at [redacted].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm

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