Official Title: *LCI-SUPP-MYE-ACUP-001*: Acupuncture for Chemo-Induced Peripheral Neuropathy (CIPN) in Multiple Myeloma (MM) Patients- A Randomized Controlled Trial

NCT04770402

IRB-Approved Date: 04/13/2023

ATRIUM HEALTH
CONSENT TO PARTICIPATE IN A RESEARCH STUDY
AND AUTHORIZATION TO DISCLOSE HEALTH INFORMATION

Sponsor / Study Title:	**Levine Cancer Institute / "Acupuncture for Chemo-Induced Peripheral Neuropathy (CIPN) in Multiple Myeloma (MM) Patients - A Randomized Controlled Trial"**
Protocol Number:	**LCI-SUPP-MYE-ACUP-001**
Principal Investigator: (Study Investigator)	**Shamille Hariharan, MD, MPH, ABOIM**
Telephone:	[redacted]
Address:	**Atrium Health** **Levine Cancer Institute-Carolinas Medical Center** [redacted]

Please read this form carefully. Take time to ask the study investigator or study staff as many questions about the study as you would like. The study investigator or study staff can explain words or information that you do not understand. Reading this form and talking to the study investigator or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must review this information, and sign and date your name at the end of this form. Participation in this study is completely voluntary.

INTRODUCTION

The study investigator listed on the first page of this form is asking you to participate in this research study at Levine Cancer Institute (LCI) and Atrium Health (AH). The purpose of this study is to see what effect acupuncture has on chemotherapy-induced peripheral neuropathy (CIPN). Peripheral neuropathy is numbness, pain, weakness, burning, or tingling in the arms/hands or legs/feet. CIPN is peripheral neuropathy caused by the effects of chemotherapy (anti-cancer treatment). This study

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is including subjects with multiple myeloma (MM) who are receiving either bortezomib (a chemotherapy agent) or bortezomib in combination with other anti-cancer medications, or have stopped bortezomib within the past twelve months, as bortezomib is known to sometimes cause CIPN. The study will enroll subjects with MM and CIPN and compare the effects of acupuncture to the effects of standard treatment on CIPN. Standard treatment is the usual care that would be recommended by your physician to treat the CIPN. You are being asked to take part because you have been diagnosed with multiple myeloma, are taking bortezomib or a bortezomib-combination chemotherapy, or have stopped taking bortezomib within the past twelve months and have symptoms of CIPN.

Depending on how severe their peripheral neuropathy is, some people may also experience a reduced quality of life, depression, poor physical function, and fatigue (tiredness). Some side effects from standard medications taken to help treat neuropathy are constipation, nausea, vomiting, sleep disturbance, and dry mouth.

Acupuncture is a possible option for treating neuropathy symptoms. It is a Traditional Chinese Medicine that involves insertion of very thin needles at specific sites on the body, known as acupoints, to affect the body's physical function and decrease pain or other symptoms. Previous studies on how acupuncture affects peripheral neuropathy have shown promising outcomes, but more information is needed. This study will help to provide more information about whether acupuncture helps to reduce the symptoms of neuropathy in subjects with MM who are on bortezomib or a bortezomib-combination treatment or have stopped taking bortezomib within the past twelve months. This research study also seeks to understand if acupuncture may lead to subjects taking less or reduced doses of pain medications, and if acupuncture may help current chemotherapy be better tolerated (less side effects).

This is a randomized, controlled study, which means you will be assigned by chance to one of two "arms" or groups of subjects. One group of subjects will be assigned to acupuncture and will receive 12 sessions of acupuncture over approximately 10 weeks, along with continued standard treatment by their physician . The other group of subjects will be considered the "control" group and will not receive acupuncture but will continue to be followed by their physician with standard treatment for their neuropathy. The randomization will be 2:1, meaning for every two subjects who get assigned to the acupuncture group, one will be assigned to the control group. The chance of you getting randomized to the acupuncture arm is 66%, and the chance of getting randomized to the control arm is 33%. The assignment (randomization) to either study arm is chosen randomly by a computer system.

If you agree to take part in the study, you will complete questionnaires either by paper form or electronically using the REDCap platform (secure web application for building and managing online surveys and databases) on a mobile device or a desktop computer.

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There will be up to 75 subjects participating in this study. Each subject will participate in the study for approximately three to four months.

WHAT WILL HAPPEN DURING THE STUDY

To participate in this study, as part of your Screening, you will need to review, sign and date this consent form and provide authorization for the release of your medical records for research purposes. By doing so, you are giving us permission to determine if you are eligible to participate in this study. You will also complete the Neuropathy 0-10 and neuropathy physical location questionnaire.

Baseline and Enrollment:

- You will be asked questions about your demographics (age, sex, race/ethnicity, health insurance type, home environment [whether you live alone or with others], marital and employment status, zip code)
- Information regarding your medical history will be collected from you and your medical records: severity of neuropathy, MM diagnosis date and stage, performance status (how well you are able to perform routine daily tasks), body mass index (BMI) with weight and height, whether you have diabetes, chronic kidney disease, vertebral fractures, or heart disease, and your current chemotherapy medication/dose/schedule
- Information on certain medications, if you are taking them, will be collected from you and your medical records (opioids, anti-inflammatory medications, some prescription medications and topical treatments, and any other medications you may be taking for treatment of your neuropathy)
- Complete questionnaires (described later in this document):
    - Acupuncture Expectancy Scale (after randomization, with subjects in the acupuncture arm only)
    - CIPN: FACT-GOG-NTX
    - Other symptoms (constipation, dizziness, dry mouth)
    - CDC HRQOL-4

After completing the consent and CIPN Neuropathy 0-10 questionnaire, if you continue to qualify for the study, you will be randomized and enrolled into the study. You will be told which "arm" you have been randomized to, which will be either the acupuncture arm or the control (no acupuncture) arm. If you are randomized to the acupuncture arm, you will begin your acupuncture sessions within two weeks of enrollment, and your CIPN will continue to be treated by your physician. If you are randomized to the control arm, you will continue to have your CIPN treated by your physician with standard treatment.

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All responses to the questions will be collected, organized, and entered into a study database. The questionnaires will not have your name attached, only a study identification number. These responses will be kept from view from other subjects and stored in a secure location. You will need to be willing to provide an active email address to which the questionnaires can be sent, if you choose to answer them electronically.

Midpoint Visit

For all subjects:
The following assessments will be repeated at week 5 (±1 week from randomization for the control arm, and ±1 week from the week of the first acupuncture session for the acupuncture arm). The questionnaires will be completed by you either in the clinic (in person, on paper), via electronic survey, or by certified mail. A phone call may be made if the questionnaires are not able to be completed by the other stated routes. The form of questionnaire administration will be based on the appointment situation, and your needs, preference, and access to a computer. These questionnaires will be completed with subjects in both arms, regardless of whether the acupuncture was received:

- CIPN: Neuropathy 0-10
- CIPN: Neuropathy physical location
- CIPN: FACT-GOG-NTX
- Other symptoms (constipation, dizziness, dry mouth)
- CDC HRQOL-4

The study staff will also ask you if there have been changes in medications you are taking.

Endpoint Visit

For all subjects:
The following assessments will be repeated at week 10 (±1 week from randomization for the control arm, and ±1 week from the week of the first acupuncture session for the acupuncture arm). The questionnaires will be completed by you either in the clinic (in person, on paper), via electronic survey, or by certified mail. A phone call may be made if the questionnaires are not able to be completed by the other stated routes. The form of questionnaire administration will be based on the appointment situation, and your needs, preference, and access to a computer. These questionnaires will be completed with subjects in both arms, regardless of whether the acupuncture was received:

- CIPN: Neuropathy 0-10
- CIPN: Neuropathy physical location

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- CIPN: FACT-GOG-NTX
- Other symptoms (constipation, dizziness, dry mouth)
- CDC HRQOL-4

The study staff will also ask you if there have been changes in medications you are taking.

Note: All subjects will complete the Midpoint and Endpoint visit assessments and questionnaires even if the bortezomib/bortezomib-combination therapy you are receiving is stopped (if applicable) during the study. Also, for subjects on the acupuncture arm, all visit assessments and questionnaires should be completed even if they have not received the acupuncture session on schedule or if sessions are missed.

Follow Up

If you are on the acupuncture arm, at approximately 30 days after your last acupuncture treatment, you will be asked if you have had any specific effects related to the acupuncture. If you do not have an appointment scheduled around this time, you will be contacted by phone for this information.

Acupuncture Arm

For subjects on the acupuncture arm, you will complete one additional questionnaire called the Acupuncture Expectancy Scale. This questionnaire is answered once prior to beginning the acupuncture visits and consists of 4 questions about your expectations regarding the effects of the acupuncture. During the Midpoint and Endpoint visits, the study staff will also ask if you have experienced some specific effects related to the acupuncture.

You will begin the acupuncture sessions within 2 weeks of enrollment into the study. Week 1 is the week of your first acupuncture session. You will receive two sessions during Weeks 1 and 2, and only one session during Weeks 3-10. During Week 1 and 2, if you miss an acupuncture session, it may be made up the following week. During Weeks 3-10, if you miss an acupuncture session, it will not be made up.

If you decide to stop the acupuncture sessions before finishing all of them, the study staff may ask if you are willing to still complete the study visits and questionnaires, as the information collected is still useful, but that will be your choice.

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ADDITIONAL INFORMATION

Questionnaires

Descriptions of the questionnaires used in this study are as follows:

- ***Neuropathy 0-10:*** This is an 11-point scale where subjects rate their neuropathy from 0-10 where 0=no neuropathy and 10=worst possible neuropathy.
- ***Acupuncture Expectancy Scale:*** This questionnaire consists of 4 questions about the subject's expectations in regard to the effects of the acupuncture.
- ***Neuropathy Physical Location:*** Subjects will be asked about the physical location of their neuropathy, with options of hands/arms only, feet/legs only, both hands/arms and feet/legs, throughout the body, and other with a write-in line.
- ***FACT/GOG-NTX:*** Subjects think back on the past 7 days and answer questions about their CIPN symptoms, physical and emotional well-being, social/family well-being, and how functional they have been.
- ***Other symptoms:*** Subjects will think back on the past 7 days and answer questions about the specific symptoms of constipation, dizziness, and dry mouth.
- ***CDC HRQOL-4:*** This questionnaire is used to measure health-related quality of life.

YOUR ROLE IN THE STUDY

Taking part in a research study can be an inconvenience to your daily life. Please consider the study time commitments and responsibilities as a research subject when you are deciding to take part. Your responsibilities as a study subject include telling the truth about your medical history and current conditions and attending the acupuncture sessions as scheduled if you are randomized to the acupuncture group.

RISKS OF THE STUDY

For all subjects: Some questions in the questionnaires could create emotional distress or confusion. Some people feel uncomfortable when answering questions about the quality of their life. Though it is always better to have fully completed questionnaires, you do not need to answer any questions that make you feel uncomfortable.

Electronic confidentiality: REDCap technology and protocols have been validated to protect your privacy and personal health information for the electronic questionnaire process. However, because personal information is being transmitted over the internet, there is still some risk of accidental disclosure of your personally identifiable medical information. Your questionnaires will be de-identified as they will contain only a subject identification number and no other personal identifiers. All of the records will be stored in a way that only allows the appropriate study staff

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access to this data. You will be notified immediately if there is any reason to believe that your privacy has been violated.

For subjects on the acupuncture arm: Information about side effects related to the acupuncture will be collected, beginning from the start of the first acupuncture session through 30 days after the last session. Let your study staff know if you experience any of these potential side effects, which include:

- Bleeding or bruising at needling site
- Edema (swelling), dry or itchy skin, hives/rash, or redness at needling site
- Skin infection at needling site
- Pain at needling site
- Dizziness
- Fainting
- Fatigue
- Sweating

There may be other study risks that are unknown.

ALTERNATIVES TO BEING IN THE STUDY

You do not need to take part in this research study. Your alternative is to continue with your physician's standard of care treatment for your CIPN with or without acupuncture outside of this study.

POTENTIAL BENEFITS OF BEING IN THE STUDY

You may or may not receive any benefit from being in the study. It is possible that you may get better, stay the same, or get worse. If you take part in this study, other people with multiple myeloma and CIPN may be helped in the future.

BEING A STUDY VOLUNTEER AND WITHDRAWING FROM THE STUDY

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, your decision will not in any way harm your relationship with your doctors or with Atrium Health. You are free to stop being in the study if you change your mind after entering it. This would not harm your relationship with your doctors or with Atrium Health.

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There is no penalty or loss of benefits to you. If you choose to withdraw from the study, please notify the study investigator.

Information already contributed to the study will remain in the study even if you choose to withdraw. If you decide to no longer participate in the study for any reason, data which may have already been collected and processed will remain de-identified and part of the study.

If you decide to withdraw this consent (decide to stop participating in this study) at any point, no further questionnaires or data will be collected from you.

Your study investigator or Levine Cancer Institute can remove you from this study for any reason at any time without your consent. Reasons include but are not limited to:

- You are non-compliant with study participation, in the opinion of the investigator (includes if you are in the control group and have an acupuncture session while enrolled)
- You withdraw consent
- You are lost to follow-up
- Your physician believes study participation is no longer in your best interest
- The study is stopped by Levine Cancer Institute

Your study investigator will explain the reasons for your removal and will help arrange for your continued care, if needed.

COSTS OF BEING IN THE STUDY

The acupuncture sessions required by the study (if you are on the acupuncture arm) are provided at no cost to you. Funding from the Carolinas Myeloma Research Fund will provide the acupuncture sessions. Visits to your medical clinic for your usual care and multiple myeloma treatment will remain your responsibility.

YOUR PAYMENT FOR BEING IN THE STUDY

You will not be paid to be in this study.

STUDY STAFF PAYMENT/FINANCIAL DISCLOSURE

None of the investigators asking you to participate in this study has received or will receive money or other benefits for personal use from the study sponsor. However, the sponsor will give money or other benefits to a research fund, foundation, educational institution, or other organization with which the investigator or study staff is associated.

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COMPENSATION FOR INJURY

In the event that you are injured as a result of your participation in this study, we will provide or arrange for treatment as necessary. This treatment, as well as other medical expenses, will be billed to you or your insurance company in the usual manner. You will be responsible for deductibles, co-payments, and co-insurance. There are no plans to pay or give you other compensation for the injury. You do not waive any legal rights by signing this consent form.

If you become ill or are hurt while you are in the study, get the medical care that you need right away.

For insurance or other payment reporting purposes, we may need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because we may have to check to see if you receive Medicare and if you do, report the payment we make to Medicare.

In no way does signing this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

CONFIDENTIALITY

The records of this study will be kept private. If any report about this research is published, we will not include any information that will make it possible to identify you. However, there is some risk that de-identified data might be re-identified. Also, your record for this study may be reviewed and/or photocopied by the Sponsor, by Atrium Health, or by representatives of the Food and Drug Administration or other government agencies.

To ensure that your information collected for this study will be kept private, your name will not be used whenever possible. A code will be used instead of your name. All your study data will be kept in a secure location.

EMAIL COMMUNICATION. By providing my email address, I give permission for Atrium Health and its representative (including third-party agents if applicable) to send me information, reminders, and messages using this means of communication. I authorize Atrium Health to send me unencrypted messages using this means of communication, and I understand and accept the risks associated with doing so. Email is not to be used for emergency situations.

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AUTHORIZATION TO USE AND DISCLOSE YOUR PROTECTED HEALTH INFORMATION

If you wish to participate in this research study, you

_____

Printed Name of Research Subject

must sign this Authorization. By signing this Authorization, you give all healthcare providers, including Atrium Health, permission to use or disclose (release) your protected health information, both past and present, for the research study described here:

LCI-SUPP-MYE-ACUP-001: Acupuncture for Chemo-Induced Peripheral Neuropathy (CIPN) in Multiple Myeloma (MM) Patients - A Randomized Controlled Trial

The protected health information that we may use or disclose (release) for this research may include all information in your medical record, such as results of physical examinations, medical history, lab tests, or certain health information indicating or relating to a particular condition.

The health information listed above may be used by and/or disclosed (released) to:

- Study investigator and research staff
- Study sponsor and/or its associated company, the Carolinas Myeloma Research Fund
- Regulatory or other governmental authorities of the United States or other countries based on this study
- Other persons or agents authorized by the study sponsor
- Atrium Health employees
- Other persons or agencies as required by law or allowed by federal regulations
- Advarra Institutional Review Board (Advarra IRB) or Data Safety and Monitoring Boards

Atrium Health is required by law to protect your protected health information. By signing this Authorization, you authorize Atrium Health to use and/or disclose (release) your protected health information for this research study. Those persons who receive your protected health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your protected health information with others without your permission, if permitted by laws governing them. Your protected health information may then no longer be protected by the Privacy Rule.

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Please note that you do not have to sign this Authorization, but if you do not, you may not receive research-related treatment through this study. However, Atrium Health may not condition (withhold or refuse) your other Atrium Health providers treating you on whether you sign this Authorization. You may change your mind and withdraw (take back) this Authorization at any time, except to the extent that Atrium Health or the Sponsor has already used or disclosed your protected health information based on this Authorization. To withdraw this Authorization, you must write to the study investigator at the address listed on the first page of this form.

No publication or public presentation about the research described above will reveal your identity without another Authorization from you. If all protected health information that does or can identify you is removed, the remaining information will no longer be subject to this Authorization or federal rules (such as the Privacy Rule) and may be used or disclosed for other purposes.

When the research for which the use or disclosure is made involves treatment and is conducted by Atrium Health: 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.

At the conclusion of the research study and at your request, you generally will have access to your protected health information. Access to your protected health information in a medical record is described in the Notice of Privacy Practices provided to you by Atrium Health.

When conducting research, the data and results may be used or disclosed for further treatment outcomes research or to research a secondary result. This Authorization will remain in effect after the end of the current study, and any future related secondary study unless it is revoked by you in writing as described above.

_____

Signature of Research Subject

_____

Printed name of Research Subject

_____

Date

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WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  [redacted]
- or call **toll free**:
- or by **email**: [redacted]

Please reference the following number when contacting the Study Subject Adviser: Pro00049444.

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.

NEW INFORMATION ABOUT THE STUDY

Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

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STATEMENT OF CONSENT

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____ ____/____/_____

Signature of Research Subject Date Time

_____

Printed Name of Research Subject

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

_____ ____/____/_____

Signature of Person Explaining Consent Date Time

_____

Printed Name of Person Explaining Consent

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