CONSENT FORM FOR RESEARCH

Study title: IIT2023-03-Vescio-ColdCap: Scalp Cooling to Prevent Hair Loss in Patients Undergoing Stem Cell Transplantation for Multiple Myeloma

Study support provided by: Internal Funding by Multiple Myeloma Research Program of Cedars-Sinai Medical Center; Penguin Cold Caps

Cedars-Sinai Principal Investigator: Robert Vescio, MD

Study contact phone number at Cedars-Sinai: Robert Vescio, MD (310) 423-1825

1. Key Information

We are asking for your consent to take part in this research study. This section provides key information about the study. The rest of this form has more detailed information.

- **Voluntary:** Taking part in this research study is your choice. You can also stop taking part at any time. You will not lose any services, benefits or rights you would normally have if you choose not to take part or stop taking part.

- **Purpose:** The purpose of this study is to determine if scalp cooling with a cold cap can reduce or prevent hair loss in multiple myeloma patients undergoing high-dose chemotherapy and peripheral blood stem cell transplantation.

- **Procedures:** The main things that will happen in this study are: A Penguin cold cap for scalp cooling will be placed upon your head by a trained technician beginning 60 minutes before and remaining for approximately 5 hours (+/- 30 minutes) after your standard of care (SOC) chemotherapy treatment with melphalan. You will receive the scalp cooling and SOC chemotherapy treatment for 2 days prior to your planned stem cell transplantation. Photographs of your hair will occur 6 times throughout the study, and a questionnaire given at 2 timepoints.

- **Duration:** Taking part in this study will last about 4 months, with up to 28 days of screening, 2 days of treatment and up to 90 days for follow up.

- **Risks:** All research studies involve some risk. Risks or discomforts from this study may be a feeling of cold and discomfort from wearing the skull cooling device. You may also develop skin irritation from the procedure. There is a privacy risk for the data collection

and photography. There is a theoretical risk of less multiple myeloma disease control in the skin cooled by the cold cap.

- **Benefits:** The possible benefits of taking part in this study are: You may lose less hair than you would have otherwise without the use of the cold cap. A successful study may help future multiple myeloma patients do something similar to prevent hair loss when undergoing this procedure.

- **Alternatives:** You can choose not to take part. There may be other choices for you. You may choose to not do the procedure and have the chemotherapy with melphalan given normally without scalp cooling. Please talk about these choices with the study team.

Please take time to read this entire form. You should ask questions before deciding whether to take part in this study. You can talk with family, friends and/or healthcare providers before you decide.

During the study, we may find out new information about this research study. We will tell you about any important changes or new findings that may impact whether you want to continue taking part in the study.

2. Purpose of the Study

We are doing this study to see if a scalp cooling treatment with cold cap (study device) is effective in reducing hair loss in patients with multiple myeloma who undergo standard of care chemotherapy with melphalan and stem cell transplantation. We want to know if the cold cap is effective in reducing hair loss and to assess the potential impact of the scalp cooling procedure.

Patients typically lose most, if not all, of the hair on their scalp after undergoing high-dose chemotherapy and stem cell transplantation for multiple myeloma. For many, the hair loss is upsetting and leads to changes in self-image and has kept some patients from choosing to undergo this potentially life-sustaining procedure. While the hair on the scalp will grow back, it typically falls out beginning 10 days after the stem cell transplant and takes 2-3 months to begin growing back. For patients with long hair, it takes quite a bit of time to return to normal. Other areas of hair such as eyebrows, typically are not as affected, presumably because hair doesn't grow very fast there.

Melphalan is the chemotherapy drug used to kill the multiple myeloma cells prior to the stem cell transplantation. It kills cells that grow and replicate quickly (like blood, intestinal and hair cells in particular). Melphalan is quickly eliminated by the body after it is given. Within 3 hours, 83% of the drug is already gone from the bloodstream. Since melphalan often causes injury to the intestinal cells resulting in mouth sores, stomach and abdominal pains and diarrhea it has become routine to have patients undergoing this treatment ingest ice chips beginning 30 minutes before and then for 3 hours after the melphalan is given to reduce these side effects. It is believed this process works by reducing blood flow to the mouth, esophagus and intestines while the melphalan concentration is at its highest. This

process has worked well and reduces mouth and intestinal problems by >50% in people using melphalan for stem cell transplantation. Given this success, it is hoped that a similar cooling of the scalp will reduce injury to hair follicles. This may work because blood vessels in the skin constrict when cold, and this should reduce the amount of blood (and therefore melphalan within the blood) from getting to the hair follicles during the time of scalp cooling. Melphalan is eliminated much more quickly than the typical chemotherapy drugs used for breast and ovarian cancer, so there is hope that scalp cooling will work especially well for those treated with melphalan. Mephalan should be > 90% gone from your bloodstream by 5 hours, the time the scalp cooling device is removed.

This device has not been approved by the U.S. Food and Drug Administration (FDA). The Cold Cap did not require FDA approval to be used in patients undergoing chemotherapy for other cancers because it is considered a nonsignificant risk device. It has been used in >20,000 patients with breast, ovarian and other cancers and has shown some reasonable success at reducing hair loss for these patients. A randomized trial in women using it during chemotherapy for breast cancer successfully prevented hair loss in 48 of 95 women using scalp cooling yet all 47 women who did not use the procedure lost their hair. It has been used routinely in patients within the Cedars-Sinai Cancer Center and hospital for patients who want to try to maintain their hair volume undergoing chemotherapy for breast and ovarian cancer. There are a few reports of successful hair preservation in patients getting stem cell transplantation, but these results have never been reported or documented in the medical literature. The Cold Cap has not been used in a medically reported fashion in patients with multiple myeloma undergoing stem cell transplantation with melphalan.

You are being asked to take part in this research study because you have multiple myeloma and have decided to undergo high-dose chemotherapy with melphalan and autologous peripheral blood stem cell transplantation.

The study will include up to 30 people in total.

3. Main Study Procedures

This section talks about what will happen in this study. When you read this section, also read the flowchart of procedures. The flowchart is given with this consent form.

The flowchart of procedures shows a timeline of the study. It shows which study procedures are research-related and which are standard of care (routine). **Research-related procedures** are procedures done only for the research study. They would not be performed for your routine care outside of the study. **Standard of care (routine) procedures** would be performed as part of your routine care even if you did not take part in this study.

Section 5 in this form describes the common medical procedures that will be done or repeated only for this research study.

Description of main research procedures:

Penguin Cold Cap Procedure:
You will receive scalp cooling with a Penguin Cold Cap, beginning 60 minutes before and remaining for approximately 5 hours (+/- 30 minutes) after your standard of care (SOC) chemotherapy treatments with melphalan. You will receive the scalp cooling and SOC chemotherapy treatment for 2 days prior to your planned stem cell transplantation.

A questionnaire about your experience will be given at two timepoints: on the day of your transplant procedure and at the end of the study.

Photography of Hair:
Additionally, a camera will be used to take pictures of the front, two sides, and back of your hair in a private clinic room by research staff at 6 times throughout the study. There will be no identifiable information and no one else visible in the images. If published, censorship bars will be used to remove any identifiable features such that only the hair is visible. The images will be stored on a computer that will not be accessible by anyone outside of the research team.

This study has 1 study group:
- Participants who will receive scalp cooling with a Penguin Cold Cap

How long will you be in the study?
We think you will be in this study for/until about 4 months. This includes up to 28 days of screening, 2 days of treatment and up to 90 days for follow up.

4. Possible Risks and Discomforts of the Main Research Procedures

This section talks about the possible risks and/or discomforts of the study procedures.

Risks of common medical procedures performed for research purposes are described below in Section 5. Side effects and risks of standard of care procedures are not described in this consent form.

Unknown Risks
There may be other risks that we cannot predict. Many complications are minor and do not last long. However, in some cases, they can be serious, long-lasting, permanent and/or fatal.

Risks of Penguin Cold Cap
There is a risk that the usage of Penguin Cold Cap could cause discomfort, a feeling of cold, or some injury to the skin or hair that would otherwise not have occurred. If the caps are applied correctly, skin irritation is rare.

There is a theoretical risk that since the procedure will reduce the blood getting to the scalp, any multiple myeloma cells present within the skin in that area would not be as fully eradicated. It should be noted that we have not seen a heightened risk for development of relapsing multiple myeloma in the mouth or intestines of patients doing ice chip administration which is routinely done and considered our current standard of care for patients undergoing stem cell transplantation. In women using this device for breast and ovarian cancer, a higher incidence of cancer recurrence in the scalp has not been seen.

There is a risk that this procedure will not work, and hair loss will not be reduced.

Risks of Stopping a Current Medication
This study requires you to stop applying any topical creams/ointments, conditioner, or oil, on the hair or scalp during the scalp cooling procedure days only. This allows these drugs to leave your body and avoids any possible conflicts with the study device effectiveness and side effects. Stopping topical medications may result in a worsening of any underlying skin condition on your scalp. Your physician will continuously monitor your condition to determine whether it is safe for you to continue in this study.

5. Common Medical Procedures Performed for Research Purposes and Risks

The procedures listed below are often part of routine care for a person with your condition. They are not experimental procedures. The procedures and their risks are research-related. This means they are being *repeated* or performed *more frequently* for this study. These common procedures and their risks should be the same as when performed outside this study.

Study Procedure	Related Risks
Medications: We will ask you about your past and current medications. Talk with the study team about any non-study medications. Non-study medications include over-the-counter drugs, supplements and vitamins.	This does not have any physical risks.
Demographic Information: We will ask you about demographics, which may include your age, gender identity, sexual orientation, race and ethnicity.	This does not have any physical risks.
Medical History Review: We will ask you about your medical history.	This does not have any physical risks.
Questionnaire: You will be asked to complete a questionnaire at 2 timepoints. We will ask you questions to find out whether the process of scalp cooling with a Penguin Cold Cap was uncomfortable or caused problems, to estimate the amount of hair loss that occurred, and whether the procedure was	Some questions may make you feel uncomfortable or embarrassed. The questionnaire will be labeled with a unique study number. This will link your identity so that only the research team can recognize you.

worth the inconvenience and annoyance. We think it should take about 10 minutes to complete each of the questionnaires.	

6. Benefits From Taking Part in the Study

Taking part in this research study may or may not have direct medical benefit to you. The possible benefits of taking part in the research study are that you may lose less hair on your head than you would have otherwise. No benefit is guaranteed. It is possible that your condition may stay the same or even get worse.

We hope the information learned from this research study will benefit other individuals undergoing chemotherapy and stem cell transplant by helping us to learn the effectiveness of scalp cooling to reduce hair loss.

7. Whether Research Results Will Be Shared

The research study uses imaging techniques that are nonstandard, using a digital camera. Therefore, imaging results obtained from this study are for research use only. We will not tell you about the results. We will not place the imaging information in your Cedars-Sinai medical record.

Unanticipated Incidental Findings
We will contact you using the last contact information you gave if, unexpectedly, we find results that suggest potentially clinically relevant medical information. We may suggest you talk with your treating physician about possible additional clinical testing to further evaluate the research finding. You and/or your insurance would pay for any additional testing and any related treatment.

8. Reasons Participation May Be Stopped

Your participation in this study may be stopped at any time. The researcher or the sponsor can stop your participation without your consent for any reason. Some reasons for stopping your participation include:

- The study is stopped or suspended.
- Funding for the study is reduced, stopped or withdrawn.
- It is in your best interest.
- You do not follow the study procedures.

9. Choosing to Take Part and Other Options

Taking part in research is voluntary. You have the right to choose not to take part. You can stop taking part in this research study at any time. You can do this without any penalty or loss of benefits to which you would be entitled outside of the study. Your choice not to take part or to stop taking part will not affect the care you get at Cedars-Sinai.

If you decide to stop taking part, we will keep any data collected on you up to the time you choose to stop. Also, if you stop taking part, the study team may ask you whether you want to give further data from your routine medical care.

You can decide not to take part in this study. You have other choices. For example, you may choose:

- To be treated following the usual clinical approach with melphalan and the stem cell transplant administered without scalp cooling being used.
- To take part in a different study at Cedars-Sinai or elsewhere, if one is available.
- To not be treated.

The study team will discuss these options and their risks and benefits with you. You may also choose to discuss these with your treating physician.

10. Confidentiality Protections

We will do our best to keep your personal information collected as part of this study private. But we cannot guarantee total privacy. We may put a copy of your research consent and authorization forms in your electronic medical record at Cedars-Sinai. Your personal information may be given out if required by law. Publications or presentations about this study at scientific meetings will not use your name and other identifiable personal information.

Organizations that may look at and/or copy your medical records for research oversight, quality assurance and data analysis include:

- Accrediting agencies (agencies that grant official certifications to educational institutions)
- Government and regulatory groups, such as the Food and Drug Administration (FDA) and Office for Human Research Protections (OHRP)
- The Institutional Review Board (IRB), which reviews research to protect people taking part in studies
- Safety monitors, which monitors the safety of individual participants and the overall safety of the study
- Companies that sponsor the study and authorized representatives of the sponsor

Attached to this consent form is an Authorization Form. It outlines with whom your information may be shared for this research and under what circumstances.

We might share your information and/or research samples collected in this study. It might be shared with other researchers at Cedars-Sinai, other academic institutions or third-party commercial entities for future research without additional informed consent from you. Information that identifies you will be removed and will not be shared with other researchers or anyone outside of Cedars-Sinai.

A description of this clinical trial will be available on 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

11. Research-Related Illness or Injury

We do not expect you will have any illness or injury from this research study. If you believe that you are ill or have been injured from this study, please contact the study team at the phone number listed on page 1 of this consent form.

12. Financial Considerations

Costs of Participation
The attached flowchart lists items, drugs and services that will be billed to you and/or your insurance and those that will be covered by the Study Sponsor. Review the flowchart for details.

For items billed to your insurance, you remain responsible for all deductibles, copays and balances under your health benefit plan. If your insurance company does not pay, you will be billed for those charges. If you have questions or concerns about your insurance coverage, you should ask your health benefit plan.

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

Financial Interest in the Research
The principal investigator and institution have no potential financial conflict of interest with this study.

13. Contact for Questions or Problems

Please contact the investigator for questions, problems or concerns about the research. Their contact information is on page 1 of this form.

You might have feedback, questions, problems, concerns or want to obtain more information about this study. If so, you can talk with someone who is not part of this study by contacting:

Cedars-Sinai Human Research Protection Program (HRPP)
Phone: 310-423-3783
Email: ResearchConcerns@cshs.org
Website: cedars-sinai.org/research/administration/office-of-research-compliance/review-board.html

The Cedars-Sinai HRPP protects the rights and welfare of research participants.

Experimental Subject's Bill of Rights

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

AUTHORIZATION FOR USE AND DISCLOSURE OF IDENTIFIABLE HEALTH INFORMATION FOR RESEARCH

1. USE AND DISCLOSURE OF HEALTH INFORMATION

If you agree to this Authorization, you give permission to the Sponsor, Principal Investigator, other investigators and their research team described in the Consent Form for Research ("Research Team") to use or disclose your identifiable health information ("private information") for the research study titled "IIT2023-03-Vescio-ColdCap: Scalp Cooling to Prevent Hair Loss in Patients Undergoing Stem Cell Transplantation for Multiple Myeloma" which is described in the Consent Form for Research ("Consent Form") to which this Authorization is attached. In particular, you authorize the research team acting under the direction of the Principal Investigator to review your medical records and collect your private information from the following sources:

- ☐ Laboratory tests
- ☐ Pathology reports
- ☐ Imaging reports (e.g., x-rays or scans)
- ☒ Photographs or videos of your image
- ☒ Doctor/clinic records
- ☒ Hospital/medical records
- ☐ Mental health records
- ☐ Billing records
- ☒ Demographics, which may include age, gender identity, race, ethnicity, and/or sexual orientation
- ☐ Other tests or other types of medical information: N/A

2. WHO WILL HAVE ACCESS TO YOUR PRIVATE INFORMATION?

Your private information will be used by and/or shared with the Research Team.

In addition to the research team, if applicable, the following parties may receive your private information and inspect your records:

- The reviewing Institutional Review Boards and Cedars-Sinai offices with authority to oversee research compliance.
- U.S. government agencies, such as the Food and Drug Administration and the Department of Health and Human Services.
- Researchers at other organizations who are participating in this research study.

- The Study Sponsor, its business partners, and Cedars-Sinai's business partners for matters related to research study oversight, conduct of the research, data analysis, use of research results in product development, and payment or reimbursement.
- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, with the Sponsor and/or the FDA.

Cedars-Sinai takes steps to protect your private information when sharing it with the recipients described above. Though these steps and applicable law are meant to protect your private information, there is a risk that a recipient could share your private information without your permission.

3. WHEN WILL MY AUTHORIZATION EXPIRE?

By signing this document, you authorize the use and sharing of your private information until the end of the research study and any related optional sub-study you choose to participate in.

4. REVOKING AUTHORIZATION

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the research team may still use or disclose private information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to the Principal Investigator of the research study by writing to the Office of Research Compliance and Quality Improvement, 6500 Wilshire Blvd, Suite 1800, Los Angeles, Calif. 90048 and/or emailing to ResearchConcerns@cshs.org.

5. NOTICE OF RIGHTS AND OTHER INFORMATION

You do not have to agree to this Authorization, but if you do not agree, you may not participate in the research study. Cedars-Sinai may not condition (withhold or refuse) the provision of standard of care treatment for you on whether you agree to this Authorization.

If you agree to this Authorization, please sign on the appropriate signature line on the Signature Page. You will receive a copy of this Authorization.

Signature Page

Consent Form for Research and Authorization
for Use and Disclosure of Identifiable Health Information (Research)

If you agree to take part in this study, you should sign and date on the signature lines below. You will be given a signed and dated copy of this form. This includes the "Experimental Subject's Bill of Rights," "Authorization for Use and Disclosure of Identifiable Health Information (Research)" and any optional sub-study descriptions, when applicable.

Signature by the Participant
Main Research Study: *I agree to take part in the research study described to me during the informed consent process and described in this informed consent form. My questions have been answered to my satisfaction.*

You will be given a signed and dated copy of this form.

Participant name (please print)	Signature	Date

Authorization for Use and Disclosure of Identifiable Health Information (Research): *I hereby agree that my identifiable health information may be used and/or disclosed in accordance with the "Authorization for Use and Disclosure of Identifiable Health Information (Research)."*

Participant name (please print)	Signature	Date

Signature by the Investigator
I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.

Investigator name (please print)	Signature	Date

Signature by the Interpreter/Witness

(Signature of an interpreter is only required when enrolling a non-English-speaking subject with the assistance of an interpreter and IRB-approved "short form" consent processes. The witness may be any person who is conversant in both English and the language of the non-English-speaking subject, such as a certified hospital interpreter, study staff, a family member or other person. The witness signs the consent forms to confirm that the oral interpretation occurred.

Signature of a witness is required when an English-speaking subjects who has been determined to have capacity to consent is unable to read or physically sign the consent form, but choses to indicate via a "mark" or verbally that he/she agrees to participate. The witness signs the consent form to confirm that an oral consent process occurred and that the individual verbally consented to participate in the research.)

Interpreter/Witness name (please print)	Signature	Date