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Topical Cannabidiol (CBD) for the Treatment of Chemotherapy-induced Peripheral Neuropathy: A Randomized Placebo-controlled Pilot Trial

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MAYO CLINIC

Name and Clinic Number
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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: Topical cannabidiol (CBD) for the treatment of chemotherapy-induced peripheral neuropathy: a randomized placebo-controlled pilot trial

IRB#: 21-011969

Principal Investigator: Stacy D'Andre, MD and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.

It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits, or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this study is to see if topical cannabidiol (CBD) can improve a chemotherapy symptom, chemotherapy-induced peripheral neuropathy (CIPN), better than placebo in patients. You have been asked to take part in this research because you have had a cancer diagnosis and you are experiencing CIPN from your treatment.
What's Involved	This study involves using a placebo cream and topical CBD cream each for two weeks. There is a 50/50 chance, like a coin flip, that you will start with a placebo instead of CBD. After two weeks you will switch to using the other cream, either placebo or CBD, depending on which treatment you used during the first two weeks. • If you can become pregnant, you will be asked to complete a pregnancy test before joining the study.

	• You will be given a symptom diary to record any symptoms you are feeling. • You will be asked to complete short questionnaires about your quality of life and neuropathy symptoms during this study. • You will be called by the study team to review your symptoms and any side effects that you are having.
Key Information	You might not benefit from this study; however, you might notice improvements in symptoms of CIPN. We hope that the information learned from this study will help future patients with symptoms like yours. You might experience skin irritation, allergic reaction, or transient worsening of your neuropathy while in this study. These side effects have been rarely reported by patients but are possible. You should not be pregnant, become pregnant, or breastfeed while in this study because we do not know how CBD can affect a baby.
Learn More	If you want to learn more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. You can discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Stacy D'Andre, MD **Phone:** (507) 284-2511 **Site Investigators:** Stephan D. Thome, M.D. (Mankato) Mina Hanna, M.D. (Albert Lea) **Study Team Contacts:** Mayo Clinic Health System Mankato Danielle Mutschler, R.N. **Phone:** (507) 594-6895 Jenna Ziegler, M.S.N., R.N. **Phone:** (507) 594-7479 Mayo Clinic Health System Albert Lea Danielle Mutschler, R.N. **Phone:** (507) 377-4817 **Institution Name and Address:** Mayo Clinic 200 First Street SW Rochester, MN 55905 Mayo Clinic Health System – Mankato 1025 Marsh Street Mankato, MN 56001 Mayo Clinic Health System – Albert Lea 404 West Fountain Street Albert Lea, MN 56007

If you have questions about …	You can contact …
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** researchparticipantadvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

Other Information:
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.

Why are you being asked to take part in this research study?

You are being asked to participate in this study because you have had a cancer diagnosis and you have chemotherapy-induced peripheral neuropathy (CIPN), or painful sensations in your hands or feet due to chemotherapy.

This study involves multiple health centers. About 40 participants will take part in this study from Sutter Health, Mayo Clinic, and Minnesota Cancer Clinical Trials Network partners. Around 40 participants may be recruited from Mayo Clinic.

Why is this research study being done?

Researchers want to see if topical cannabidiol (CBD) can improve CIPN better than placebo in patients. Patients who have had chemotherapy that caused neuropathy may be able to participate in this trial.

CIPN is commonly seen in patients receiving certain chemotherapy medications and is hard to treat. Medications commonly used to treat CIPN have limited benefits and may cause significant side effects. A small report showed that topical CBD may help treat neuropathy in patients with diabetes. This study is being done to determine if CBD cream can help improve the symptoms of CIPN.

For more information about herbal supplements, including CBD, a good resource is the National Center for Complementary and Integrative Health, a division of the National Institutes of Health (*https://nccih.nih.gov/*).

Information you should know

Who is Funding the Study?
The Breast Cancer Research Foundation (BCRF) is funding this research. Placebo and CBD creams will be provided by Nightingale Remedies.

Information Regarding Conflict of Interest:
Your healthcare provider may be referring you to this research study. If your healthcare provider is also an investigator on this study, there is the chance that his or her responsibilities for the study could influence his or her recommendation for your participation. If you prefer, your healthcare provider will be happy to refer you to another investigator on the research study team for you to decide if you want to participate in the study and to see you for the research study activities while you are in the study.

How long will you be in this research study?

If you agree to take part in this study, your total involvement time could last approximately one to two months and will consist of seven interactions. You will be asked to use the study creams for a total of four weeks. The interactions will occur at normally scheduled office visits or through a phone call.

What will happen to you while you are in this research study?

If you agree to be in this study, you will be asked to participate in the following:
Interaction 1:

- A review of your medical history, medications & answer questions about your nerve symptoms.
- You will be asked to complete a Questionnaire packet including: EORTC QLQ-CIPN 20 instrument, Chemotherapy Induced Peripheral Neuropathy Assessment Tool & a Symptom experience diary.
- You will be "randomized" into one of the two study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you will be in. You will have an equal (50/50) chance of being placed in either group.
- Half of the patients will be assigned to the active treatment group with cream containing the study product CBD, and after two-weeks cross over to cream that contains only placebo.
- Half of the patients will be assigned to the placebo group with cream that does not contain the study product CBD, and after two-weeks cross over to cream containing the study product, CBD.

Interaction 2 (which may happen on the same day as interaction 1):

- You will be given the CBD or placebo cream.
- You will be given four questionnaire packets, each including: the EORTC QLQ-CIPN 20 instrument, a Global Impressions of Change questionnaire, a Chemotherapy Induced Peripheral Neuropathy Assessment Tool & a Symptom experience diary; you will be provided with packaging to ship questionnaire packets back at the end of weeks two and four.

Interaction 3 (at the end of week 1) – Phone Call:

- You will be called to review any side affects you may be having and to answer questions about your nerve symptoms.
- You will be asked to complete a questionnaire packet previously provided.

Interaction 4 (at the end of week 2) – Phone Call or Visit:

- You will be called to review any side affects you may be having and to answer questions about your nerve symptoms.
- You will be asked to complete a questionnaire packet previously provided.
- You will be given a new CBD or placebo cream to use (whichever one you did not receive previously).
- You will be asked to return your first two weeks of questionnaire packets during visit or in the postage paid packaging provided to you previously.

Interaction 5 (at the end of week 3)– Phone Call:

- This will be the same as interaction 3.

Interaction 6 (at the end of week 4)– Phone Call:

- This will be the same as interaction 3.

Interaction 7 (which may happen on the same day as interaction 6):

- You will be asked to return your second two weeks of questionnaire packets (all four if not previously sent) in the postage paid packaging provided to you previously.

This study uses a placebo. A placebo looks exactly like the study drug, but it contains no active ingredient. We use placebos in research studies to learn if the effects seen in research participants are truly from the study drug.

During this study, we will ask you to fill out questionnaires about your neuropathy symptoms and quality of life. We hope that you will answer all the questions, but you can skip any questions you don't want to answer. Each questionnaire should take only a few minutes to complete.

What are the possible risks or discomforts from being in this research study?

While participating in this study you may experience skin irritation, allergic reaction, or transient worsening of neuropathy. These side effects have been rarely reported by patients but are possible.

There is a chance that a very small amount of CBD will be absorbed into the bloodstream. This is much less than the amounts that are typically taken by mouth. There are no reported side effects in the literature using similar topical creams. Side effects of higher dose CBD when taken by mouth include nausea, diarrhea, fatigue/sedation, suicidal behavior, and ideation and change in liver function tests.

The effect of CBD on a developing baby still in the womb, or on a breastfed infant, is unknown and may be harmful. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding. If you are a female who can become pregnant, you must have a negative pregnancy test to participate in this study. There may be other risks of CBD that are currently unknown.

In all research there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the study team if you decide to stop.

The Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- If it is in your best interest
- If you don't follow the study procedures
- If you develop any side effects to the study treatment

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study, if such becomes known.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for any research-related injuries from this study will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments, and coinsurance.

What are the possible benefits from being in this research study?

You might not benefit from this study. However, potential benefits may include improvements in symptoms of CIPN. We also hope that the information gained from the study will help in the treatment of future patients with conditions like yours.

What alternative do you have if you choose not to participate in this research study?

You don’t have to be in this study to receive treatment for your condition. Your other choices may include medical treatments that your doctor may prescribe such as gabapentin or duloxetine, or acupuncture. Some patients choose to use cannabis creams available commercially, however these have not been tested in a clinical trial. Talk to the Principal Investigator or your doctor if you have any questions about any of these treatments or procedures.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- CBD or placebo creams
- Shipping materials to return questionnaire packets once the study is over
- Activities done as part of the described study interactions
- Pregnancy test

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You will not be paid for being in this research study**.**

Will your information or samples be used for future research?

Your information or samples collected for this study may be used or shared for future research studies. If used or shared, identifiable information such as your name, Mayo Clinic number or date of birth will be removed to protect your privacy.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you for this research study.

Various methods are used to safeguard your confidentiality. The following methods may be used in this study: assigning a unique code or registration number to your data and samples, storing research materials in locked areas, and storage of encrypted, password-protected data on a computer.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present, and future medical records.
- Research procedures, including research office visits, tests, interviews, and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health, and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.
- The Minnesota Cancer Clinical Trials Network (MNCCTN) for participants enrolled at Mayo Clinic Health System sites.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you.

This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports, or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic, or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: researchparticipantadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

Printed Name Date (mm/dd/yyyy) Time (hh:mm am/pm)

Signature