Title: Pilot Studies Testing the Effect of Topical Imipramine on Pain and Effectiveness of Topical Photodynamic Therapy

NCT #: NCT05688904

Document Type: Informed Consent

Document Date: 06FEB2023

WRIGHT STATE UNIVERSITY

Pharmacology Translational Unit

Wright State Physicians

INFORMED CONSENT FORM AND AUTHORIZATION FOR RESEARCH

Pilot Studies Testing the Effect of Topical Imipramine on Pain and Effectiveness of Topical Photodynamic Therapy

PI: Craig A. Rohan, M.D.

Departments of Pharmacology & Toxicology and Dermatology

About This Research Study

You are asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future. This consent form will give you information about the study to help you decide if you want to participate. The study staff will discuss this study with you and explain everything in detail. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

This study is being conducted by: Dr. Craig Rohan, MD, Assistant Professor of Pharmacology & Toxicology, assisted by Dr. Jeffrey B. Travers, MD, PhD, Chair of Pharmacology & Toxicology.

This study is being funded by: The study will be funded by the Wright State University Department of Pharmacology and Toxicology through a grant from the US National Institutes of Health.

Key Information

The purpose of this consent form is to give you information about this research study. It is up to you to decide whether to take part in this study. If you choose not to participate, your decision will not affect your current or future relationship with Wright State Physicians. If you decide to participate, you are free to withdraw at any time without affecting that relationship.

The purpose of this study is testing the use of topical Imipramine in combination with topical photodynamic therapy's (PDT) effect on pain following treatment. PDT is a commonly used treatment in dermatology for patients who have many pre-cancers (actinic keratosis-AKs) on their skin. These are both FDA-approved treatments, but this study is evaluating their use in combination, which has not been evaluated in the past. The investigators have been doing studies using animals that suggest that imipramine might make the PDT less painful and might help it work better. You and your dermatologist have decided that you would benefit from PDT to treat your skin due to many AK precancerous lesions. Please note that neither PDT nor imipramine are experimental treatments, but treating your skin with imipramine before PDT is a new approach. There is a separate informed consent for the PDT.

If you agree to be in this study the following will happen:

- We will obtain a list of all your current medications
- The PDT site(s) will be photographed. These pictures will include a digital photo, a thermal imaging photo, and a photo with a dermachrome card
- We will count the numbers of precancerous actinic keratoses on the areas

- Imipramine and control liquid each will be applied to half of the areas to be treated
- Blue light will be exposed to your forearms or face/scalp for 16 minutes and 40 seconds
- We will ask you to rate your Pain and Itch

Your participation in this study will take up to 6 months

Potential risks you may experience include:
- The imipramine or control liquids could make the PDT treatment more painful or less effective in treating the precancerous actinic keratoses.
- Additional risks can be found on page 5

You may not benefit by participating in this study. However, the information gained may be helpful to others.

The alternative to participating in this study is to not participate.

Why is This Study Being Done?
The purpose of this study is to test if the combination of topical Imipramine applied to the forearms or face/scalp prior to PDT will improve your pain following therapy.

Why Am I Being Asked to Participate in This Research Study?
You are asked because you are 18 years or older and have fair skin (Fitzpatrick types I – III) and have been prescribed PDT by your doctor.

How Many People Will Take Part?
If you agree to participate, you will be one of approximately 24 participants who will be taking part in this study.

Taking Part in this Study is Voluntary
You may choose not to take part in this study or choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled. Your decision to participate or not in this study will not affect your current or future relationship with Wright State Physicians, nor will it affect your health care. If you decide to participate, you are free to withdraw at any time without affecting that relationship. Please read this entire consent form and take your time to make your decision. We encourage you to talk to your doctor, your family, and/or your friends before you decide.

What Will Happen During the Study?
If you agree to be in this study the following will happen:

DURING THE STUDY
This research will take place at the Pharmacology Translational Unit, Wright State Physicians Building. The study is being conducted under the direction of Dr. Craig A. Rohan, Principal Investigator.

Visit 1/Day 1 (Approximately 3-4 hours)
1. Pictures will be taken of the planned PDT treatment sites. Please note that pictures taken during this study include digital photos, photos with a dermachrome card and thermal imaging photos. A dermachrome card allows computers to assess scattering properties of skin.
2. Precancerous areas (AKs) will be counted and mapped (arms or face/scalp).
3. We will measure redness of the sites with a non-invasive probe that touches your skin (Mexameter).

4. We will have you fill out pain and itch scales for the middle areas of each forearm or half of face/scalp. Pain and itch will be individually assessed using a 0-100 mm visual analog scale (VAS) for each. You will draw a small line on the VAS diagram to reflect your assessment of pain and itch. 0 mm being no pain or itch. 100 mm being the worst pain or itch imaginable.
5. The routine PDT treatment and application of appropriate and standard amounts of the agent called 5-ALA which makes your skin more sensitive to light, Ameluz 10% gel or a Keratostick, with the photosensitizing agent 5-aminolevulinic acid (5-ALA) to each forearm, or face/scalp, and potentially cover (if needed) with a large non-adherent dressing. You will be allowed to leave the clinic at this time but must return in 1 hour.
6. **1 Hour After 5-ALA Application**: You will return and complete the VAS scales. Then we will then apply Imipramine and liquid vehicle each to one side of the face/scalp or your forearms for 1 additional hour. The liquids will be labelled "1" and "2" and neither you nor the investigators will know which side has the active imipramine or the control liquid. Approximately 1 ml of liquid (1/5th of a teaspoon) will be applied per treated area.
7. **1 Hour After Study Agent Application**: You will complete the VAS scales. Then standard PDT will be performed by the Dermatology Department. We will treat the areas with the blue light source for 16 minutes and 40 seconds. If forearms are involved, this will take a total of 34 minutes as we are doing one forearm at a time. Your eyes will be covered with lead shields and we will have small fans running over the areas to decrease the mild burning sensations.
8. We will have you fill out a second pain and itch scale for the middle areas of each forearm or half of face/scalp. These measurements of pain and itch will be recorded by you for each side after PDT is completed and at 10 minutes and 30 minutes. Pain and itch will be individually assessed using a 0-100 mm VAS for each. You will draw a small line on the VAS diagram to reflect your assessment of pain and itch. 0 mm being no pain or itch. 100 mm being the worst pain or itch imaginable.
9. Additional photographs and redness readings will also be obtained at 10 minutes and 30 minutes after the blue light treatment.

Visit 2/Day 2 (Approximately 60 minutes)

1. We will take pictures and redness measurements of the PDT treated sites.
2. We will have you fill out Pain and Itch scales for each treated area as noted in Visit 1.

Visit 3/Day 180 (+/- 14 Days six months after treatment/End of Study - Approximately 60 minutes)

1. We will take pictures of the PDT treated sites.
2. Count precancerous areas (AKs) in the PDT treated sites with a map

What Steps Are Being Taken to Reduce Risk of Coronavirus Infection?

We comply with all health mandates set forth by Wright State Physicians. When applicable, the unit complies with federal, state and local health mandates as well.

How Long Will I Be in This Research Study?

If you choose to take part, you will be in the study for 6 months from the first Screening Visit through the final follow-up procedures.

Can I Stop Being in This Research Study? What Happens if I Change My Mind?

If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without any penalty. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled

The principal investigator or study staff may also withdraw you from the study, without your consent for one or more of the following reasons

- Failure to follow the instructions of the research study staff.
- You need treatment not allowed in the study.
- The study is cancelled.
- The principal investigator believes it is in your best interest.

Is There Any Way Being in This Study Could Be Bad for Me? What are the Risks?

This research may hurt you or cause discomfort in the following ways:

- PDT Treatment: PDT results in a localized sunburn-like reaction. You and your dermatology provider have decided that PDT is the best treatment for your sun damage and pre-cancerous skin lesions. The reactions can be associated with some itch and minimal pain. It is possible that you could experience a severe reaction, including blistering. If you are symptomatic, Drs. Rohan and Travers, Board-Certified Dermatologists, will evaluate whether additional treatments (e.g., addition of topical corticosteroids) are needed. An advantage to the design of the study is that you will be returning at 1 day post-treatment for redness measurements/pain scales to allow Drs. Rohan and Travers to inspect the areas. Please note that the PDT is not experimental and is standard care for precancerous lesions. **You need to use sunscreen or wear long-sleeved shirts for 3 days after the PDT treatment.**
- Imipramine: Topical use of imipramine is unlikely to cause any of the harmful effects/side effects listed with oral use. It has not been tested in the current way. This drug is used either by mouth or by topical use to treat many conditions, including pain. It is possible that the blue light, as part of the PDT treatment, might cause increased reactions such as sunburn to your skin. However, our testing in cell lines and in mice suggests the opposite – that it decreases the inflammation and pain from PDT. There is a risk of allergic reaction to imipramine, or other inactive ingredients in the liquid formulation which is treatable.
- Topical 5-aminolevulinic acid gel (Ameluz) or liquid (Keratostick): This agent is a photosensitizer. It can cause increased sunburn-like reactions. You need to avoid bright sunlight and no tanning beds for at least 3 days after the PDT treatments. You need to use sunscreen or wear long-sleeved shirts for 3 days after the PDT treatment.
- There are no risks to photography, nor mexameter readings, nor pain/itch scales. Photographs will not allow you to be recognizable.
- Loss of Privacy**:** A risk of this research is a loss of privacy (revealing to others that you are taking part in this study) or confidentiality (revealing information about you to others to whom you have not given permission to see this information). However, this will be minimized as photographs will be labelled with numbers only. The study number XXXXX followed by 01, 02, 03, etc. See the section, titled “How Will my Information be Protected.”

What Do I Need to Know About Reproductive Health and/or Sexual Activity if I Am in This Study

Careful consideration should be taken if you are currently pregnant or plan to get pregnant or father a baby or breastfeed or donate eggs/sperm while on this research study. Once you complete the study, there is not a set amount of time you should wait before becoming pregnant or father a child.

If you are sexually active, both men and women should use at least one effective means of birth control while participating in this research study. According to the World Health Organization and the United States Center for Disease Control and Prevention, the most effective forms of birth control include complete abstinence, surgical sterilization (both male and female), intrauterine devices (IUDs), and the contraceptive implant. The next most effective forms of birth control include injectables, oral contraceptive pills, the contraceptive ring, or the contraceptive patch. Acceptable but least effective methods of birth control include male condoms (with or without spermicide) and female condoms.

If you or your partner become pregnant while participating in this research study it is important that you inform the study doctor or other research team member.

What are the Potential Benefits of Taking Part in the Study?

The benefit to participation is possible pain reduction after receiving PDT. More broadly, this study may help the researchers learn more about the best approaches to treat sun damage and precancerous lesions. This may help other patients and other researchers in the future.

Will I Receive My Research Results?

We will not be obtaining any results from the study activities which could be important to your health or well-being.

Will I Be Told About New Information That May Affect My Decision to Participate in This Research Study?

During the course of the study, you will be informed of any significant new research information (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might cause you to change your mind about continuing in the research. If new information is provided to you, you may be asked to sign a consent form that includes the new information.

Will I be Paid to Participate in the Research?

You will receive $100 as payment for your participation. You will be given payment after Visit 2 and Visit 3. You will be given partial payments if you are unable to complete the entire study as outlined below:

- Visit 1
  - Informed Consent - $20
  - Photographs, Counting AKs, pain/itch scales and redness readings - $20
  - Imipramine/control treatment - $20
- Visit 2: Photographs and redness readings and completion of Skin Pain and Itch Scales - $20
- Visit 3: Photographs, Counting AKs - $20

Subjects are not required to accept compensation. If compensation is not accepted, it will be retained for future subject compensation.

Will It Cost Me Anything to Participate?

There is a cost associated with your PDT that is billed through your insurance. There is no added cost by taking part in this study and patients who complete the study will receive payments as noted in the previous section.

Who Will Pay for My Treatment If I Am Injured?

Emergency Contact (24 hour): [redacted]

If you feel that you have been injured as a result of participating in the research, contact the research office at (937)-245-7500 to talk about your illness or injury. If you are injured by being in this research study, you will be treated appropriately with no physician cost from Dr. Travers/Dr. Rohan, though a pharmacy fee could be incurred if prescriptions are required. Also, it is your responsibility to determine the extent of your health care. coverage. The study sponsor does not plan to provide other forms of compensation (such as lost wages or pain and suffering) to you for research related illness or injury. By signing this form, you will not give up any legal rights.

How Will my Information Be Protected?

The people who will know that you are a research subject are members of the research study staff, and if appropriate, your physicians and nurses. No information about you, or provided by you during the research, will be disclosed to others without your written permission, except if necessary to protect your rights or welfare or if required by law.

The information that you give in the study will be handled confidentially. Your information will be assigned a subject number.

Your data/subject chart will be stored in locked cabinets and a secure cloud-based storage system. This informed consent form will be kept for a minimum of 6 years after the study is complete, then it will be archived.

It is unlikely, but possible, that others responsible for research oversight may require us to share the information you give us from the study to ensure that the research was conducted safely and appropriately. Organizations, in addition to the Wright State Institutional Review Board (IRB) and research investigators, that may inspect your research records include Wright State Physicians and the Office of Human Research Protections (OHRP). We will only share your information if law or policy requires us to do so. If the researchers learn that you are abusing/neglecting/going to engage in self-harm/intend to harm another, state law requires the researchers report this behavior/intention to the authorities. Finally, confidentiality could be broken if materials from this study were subpoenaed by a court of law.

FDA Clinical Trial Registry

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.

Authorization to Use and Disclose Your Health Information

State and Federal laws, including the Health Insurance Portability and Accountability Act (HIPAA), require researchers to protect the privacy of your health information. This section of the consent form describes how researchers, with your authorization (permission), may use and release (disclose or share) your protected health information (PHI) for this research study. **Please read this section of the consent form carefully.**

If you sign this document, you give permission to Dr. Craig Rohan and his Wright State Physicians Pharmacology Translational Unit research team to use or disclose (release) the following protected health information:

- Your medical records for past medical conditions and medications related to your skin health/condition
- All information (research records and medical records) created during your participation in this research study
- All information related to illness or hospitalizations that occur during your participation in this study

The research team needs this information to conduct the study. This is a study to test if topical Imipramine used in combination with PDT effects pain post treatment.

To maintain the integrity of this research, you might not have access to any health information developed as part of this study until it is completed. At that point, you generally would have access to your health information.

Disclosure of your protected health information

If you sign this form, the researchers may share your health information during the conduct of the study with:

- Non-Wright State Physicians researchers or organizations working with Wright State Physicians researchers.
- Law enforcement or other agencies, when required by law
- Wright State University Institutional Review Board, which oversees our research
- The sponsor (the organization paying for) of this research study: National Institutes of Health
- Representatives of government agencies in the United States and other countries (i.e. Food and Drug Administration and the Office of Human Research Protection)
- Other authorized Wright State Physicians Officials who oversee research and clinical care

The people listed above will use and share your health information to review the quality, safety, and results of the research and may also do additional research.

Please understand that these persons/organizations who may receive your health information may not be required by U.S. Federal privacy laws (such as HIPAA) to protect it and may share your information with others without your permission.

This authorization does not have an expiration date.

However, you can change your mind and cancel this authorization at any time. To cancel this authorization, you must write to the principal investigator at 725 University Blvd., Fairborn, OH 45234.

If you cancel this authorization, you will no longer be allowed to take part in the research study. If you cancel this authorization, health information you had already allowed us to obtain may still be used and disclosed by researchers in order to maintain the integrity and reliability of the research, and to report any adverse (bad) effects that may have happened to you.

Right to Refuse to Sign this Authorization
You have the right to refuse to sign and give your authorization. If you do not sign this form, your non-research-related treatment, payment or enrollment in any health plans, or your eligibility for other medical benefits at Wright State Physicians will not be affected in any way.

However, if you do not sign this form, you will not be able to participate in this research study.

Will My Information Be Used for Research in the Future?

Information collected from you may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information is shared.

Who Should I Call with Questions?

If you have questions about the research study itself, please contact the Principal Investigator at (937)245-7500. If you have questions about your rights as a research volunteer or would simply like to speak with someone other than the research team about concerns regarding this study, please contact the Wright State IRB Office at (937) 775-4462 or irb-rsp@wright.edu. All reports or correspondence will be kept confidential.

You will be given a copy of this information to keep for your records.

What Are My Rights/Responsibilities As A Research Subject?

As a subject, your responsibilities include:

- Follow the instructions of the research study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the research staff if you believe you might be pregnant or have gotten your partner pregnant.
- Complete your questionnaires as instructed.
- Ask questions as you think of them.
- Tell the research staff if you change your mind about staying in the study.

While participating in this research study, you should not take part in any other research project without approval from the research staff of each study.

Statement of Consent

I have read (or someone has read to me) the above information provided in this form. I have had the opportunity to ask questions and have my questions answered. In consideration of all information provided in this form, I give my consent to participate in this research study and authorize the use and disclosure of my protected health information for this study. I will be provided with a copy of this form to keep for my records.

I agree	**I disagree**	
_____	_____	The researcher may take photos of me to aid with data analysis.
_____	_____	The researcher may take photos of me for use in scholarly presentations or publications. My identity may be shared as part of this activity, although the researcher will attempt to limit such identification. I understand the risks associated with such identification.
_____	_____	The researcher may contact me in the future to see whether I am interested in participating in other research studies by the Principal Investigator of this study.

Signature of Subject

Your signature documents your permission to take part in this research. You will be provided with a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent