The Effect of Abobotulinum Toxin A on the Symptoms of Raynaud's Phenomenon, a Double-Blind Randomized Placebo-Controlled Trial

NCT03639766

Date: May 21st, 2019

The Effect of Abobotulinum Toxin A on the Symptoms of Raynaud's Phenomenon, a Double-Blind Randomized Placebo-Controlled Trial

Informed Consent

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Investigational Site(s):	UCF Health Clinic, 9975 Tavistock Lakes Blvd, Orlando, FL 32827, (407) 266-4900

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you have a current diagnosis of Raynaud's phenomenon, a disease the is characterized by the spasm of the blood vessels in the fingers, and you have health insurance. You must be 18 years of age or older to participate in this study.

You cannot be in this study if: (1) you are allergic to abobotulinum toxin A or its components, (2) you have a diagnosis of myasthenia gravis; (3) you are unable to read and speak English, (4) you are pregnant or breastfeeding, (5) you have previously received botulinum toxin vaccine, (6) you have previously undergone upper extremity vascular surgery, (7) you have previously received abobotulinum toxin A treatment in either hand in the past 6 months, (8) you are a current smoker or quit in the past 12 months, or (9) you are a prisoner.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team by phone at (407)266-3627 and ask for Dr. David Weinstein MD, UCF College of Medicine, UCF Health, or by e-mail at david.weinstein@ucf.edu .

This research has been reviewed and approved by an Institutional Review Board ("IRB"). You may talk to them at 407-823-2901or irb@ucf.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

Background and Purpose: Raynaud's phenomenon is a debilitating disorder where circulation in the extremities, like the fingers and toes, is severely reduced. Although botulinum toxin (BoNT) is most well-known for its cosmetic uses, studies have shown it provides relief from symptoms for patients suffering from Raynaud's. Studies have shown that BoNT improves blood flow in the hands as well as reduces pain and improves function. However, studies have focused on specific patient population and lacked coordinated methodology. Abobotulinum toxin A, a type of botulinum toxin, is currently FDA-approved for cervical dystonia, moderate to severe glabellar lines, upper limb spasticity, and lower limb spasticity. But it is not approved to treat the symptoms of Raynaud's phenomenon. Only a few clinical trial studies have been done with several of them supporting the use of this drug to treat this medical condition. As there is no drug approved specifically for treating Raynaud's phenomenon this treatment may benefit you. However, FDA has not determined that the drug is safe and effective for the treatment of your condition. Our double-blind randomized placebo-controlled trial seeks to compare a BoNT group with a placebo saline group, studying the effect of abobotulinum toxin A (a type of botulinum toxin A) on Raynaud's symptoms among a more diverse population to provide insight into the patients most likely to benefit from BTX.

How long will the research last?

We expect that you will be in this research study for 12 months, including one 1-hour appointment and four 15-minute follow-up appointments at UCF Health. You will also be asked to complete weekly or monthly progress surveys during the study duration.

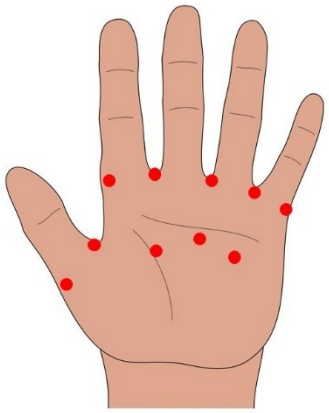
How many people will be studied?

We expect about 20 people here will be in this research study.

What happens if I say yes, I want to be in this research?

- You will not be required to discontinue any of your current medications
- Upon arrival at UCF Health, you will have time to read, ask questions and fill out this consent form before participation.
- After you sign this consent form you will be asked a series of questions regarding your health history to determine if you are eligible to participate in this study.
  Note: If you are female, you may need to provide a urine sample for a pregnancy test to determine if you are eligible to participate in this research study. The reason for this is because one of the drugs you will receive as part of this study is abobotulinum toxin A, and even though the dose is very small (300 units), the effects of abobotulinum toxin A on an embryo or fetus are not known. The urine pregnancy test must be negative for you to participate in the study.

- If you continue to be eligible to participate in the study the following will occur:
- Day 0:
  - You will be asked to fill out a baseline questionnaire, which includes questions that assess the symptoms of your Raynaud's.
  - You will be evaluated by Dr. David Weinstein.
  - Photographs will be taken of your hands.
- You will receive 20 small injections, 10 on each palm, administered by Dr. David Weinstein. 1ml will be injected in each location. The abobotulinum toxin A solution will consist of 30 units abobotulinum toxin A per ml and the normal saline solution will consist of 0.9 % sodium chloride.



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  - You will be asked to wait 20 minutes after injection to be observed for any reactions.
- 48 hours after injections:

    - You will receive a follow up phone call from Dr. Weinstein 48-hours after the injections to make sure you are doing well
- 1-month follow-up:
    - You will be evaluated, asked to complete a questionnaire in person, and have your hands photographed
- 3-month follow-up:
    - You will be evaluated, asked to complete a questionnaire in person, and have your hands photographed
- 6-month follow-up:
    - You will be evaluated, asked to complete a questionnaire in person, and have your hands photographed
- 12-month follow-up:
    - You will be evaluated, asked to complete a questionnaire in person, and have your hands photographed
- In addition, you will be asked to complete a survey either online or in paper every week for the first 3 months and then every month for the final 12 months.

The treatment you get will in each hand be chosen by chance, like +ipping a coin. Neither you nor the study doctor will choose which treatment each hand will receive. Each hand will have an equal chance of being given each treatment, though only one hand will receive the treatment with abobotulinum toxin A. Neither you nor the study doctor will know which treatment which hand is getting.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

- Receive a one-time set of 20 injections (10 per hand) at your first visit
- Attend five in-clinic appointments and answer a 48-hour follow-up phone call
- Answer truthfully questionnaires given to you at your in-clinic appointments
- Complete paper or online questionnaire weekly during your first 3 months in the study and then monthly for the final 9 months

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate or not to participate.

Instead of being in this research study, your choices may include: continuing to receive your current care for Raynaud's phenomenon with your rheumatologist or dermatologist.

The important risks and possible benefits of these alternatives include:

- No change or possible progression of your Raynaud's phenomenon.

What happens if I say yes, but I change my mind later?

You can leave the research at any time. It will not be held against you.

You can withdraw from the study at any time during the study by contacting the principal investigator or co-investigators. If you decide to leave the research, no further data will be collected from you and you are free to leave. However, partial data already collected will be used for analysis. There will be no consequences for your choice to leave. If you decide to leave the study, contact the investigator so that the investigator can stop recording data from you.

Is there any way being in this study could be bad for me?

Risks: This study is considered more than minimal risk because of the injection you will receive, however there are no major anticipated risks associated with the study. Potential risks include:

- Discomfort and minimal pain upon injection and infiltration of abotulinum toxin A/saline
- Temporary muscle weakness that may last 6 weeks
- Negligible bleeding or bruising
- Risk of infection (<1%)
- Allergy to abobotulinum toxin A solution (<1%)

There may be uncommon or previously unforeseen risks. You should report any problems to the researcher immediately.

Note: DO NOT take part in this study if you are known to be allergic to abobotulinum toxin A.

If you do suspect that you are having any adverse reaction, please contact Dr. David Weinstein. He can be reached via e-mail at david.weinstein@ucf.edu or by phone at UCF Health at (407)266-4900. If you need emergency care, call 911 or go to your nearest hospital or emergency room right away. It is important that you tell the doctors at the hospital or emergency room that you are participating in this research study. If possible, take a copy of this consent form with you when you go.

The procedures in this research are known to hurt a pregnancy or fetus in the following ways:

DYSPORT® produced embryo-fetal toxicity in relation to maternal toxicity when given to pregnant rats and rabbits at doses lower than or similar to the maximum recommended human dose (MRHD) of 1000 Units on a body weight (Units/kg) basis. The research may also hurt a pregnancy or fetus in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death. You should not be or become while on this research study.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include relief from your Raynaud's symptoms. This relief may only be temporary and only last a few months.

What happens to the information collected for the research?

We will limit your personal data collected in this study to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of UCF. There is the possibility that the Food and Drug Administration (FDA) and/or the Office for Human Research Protections (OHRP) may inspect the research records.

Monitors, auditors, IRB, and regulatory authorities will be granted direct access to the participant's original medical records for verification of clinical trial procedures and data, without violating the confidentiality of the participant, to the extent permitted by applicable laws and regulations and that, by signing the consent document, the participant or the participant's legally authorized representative is authorizing such access.

If the results of the trial are published, the participant's identity will remain confidential.

Your name and contact information will be coded. Your unique identifier will be stored in a separate folder in locked drawer in a locked room at UCF Health. Data will be stored in locked drawer in a locked room at UCF Health and kept for a minimum of six years after the conclusion of the study (per UCF data retention policies.) We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

Federal law provides additional protections of your medical records and related health information. These are described in an attached document.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include:

- failure to follow instructions from staff
- adverse reaction to one of the solutions
- The principal investigator ends the research study early

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

You will not be compensated for your time (approximately 2.5 hours) and will have to bear any transportation costs (gas, tolls, etc.). If your health insurance does not cover the costs for treatment related injury, you may be billed for the treatment.

If you need medical care because of taking part in this research study, contact the investigator and medical care will be made available. Generally, this care will be billed to you, your insurance, or other third party. UCF Health has no program to pay for medical care for research-related injury. In the event that you suffer a research-related injury, your medical expenses will be your responsibility or

that of your third-party payer, although you are not precluded from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research.

You will be informed about the results of the study when we have completed data collection and published our results in a scientific journal.

You will be provided with a copy if this signed consent, in case you want to read it again.

You have to additional sign the UCF Health HIPAA Authorization to start your participation in this study.

Signature Block for Capable Adult

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

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	