INSTITUTE: National Cancer Institute

STUDY NUMBER: 15-C-0142 PRINCIPAL INVESTIGATOR: Staci Martin Peron, PhD.

STUDY TITLE: Acceptance and Commitment Training for Adolescents and Adults with Neurofibromatosis Type 1, Plexiform Neurofibromas, and Chronic Pain: A Phase III Clinical Trial

Continuing Review Approved by the IRB on 03/13/19

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Standard



## INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary**.**

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

If you are signing for a minor child, "you" refers to "your child" throughout the consent document.

**Why is this study being done?**

The primary purpose of this study is to test whether a type of therapy called Acceptance and Commitment Therapy (ACT) can help people with neurofibromatosis 1 (also called NF1) cope better with the pain associated with NF1. ACT is a type of therapy that focuses on things like values (who and what is important to you) and living in the present moment. This study will see

whether participating in an intervention based on a variety of ACT techniques improves pain and coping in people with NF1 pain after an 8-week ACT intervention.

Usual methods of treating pain include medications, such as over the counter medications and prescription pain relievers, and behavioral treatments, such as relaxation exercises. Because we want to test if ACT intervention works better than these usual methods, we will randomly assign participants to the ACT group OR to a 'wait-list' group. This means you have equal chance of being in the ACT group or the 'wait-list' group, similar to flipping a coin. The ACT group will start the ACT intervention immediately while the 'wait-list' group will continue doing whatever they usually do to cope with their pain. After the 8-week intervention, everyone will return to NIH for follow-up evaluations. At that time, the 'wait-list' group will start the ACT intervention.

In this study, we will use a set of questionnaires and a heart rate test, called electrocardiogram (ECG), to assess pain and coping before starting the ACT intervention and then after the 8-week program to see if there are any changes in your heart rate. Everyone will complete a final set of questionnaires from their home computer, tablet, or smartphone 6 months after the formal ACT intervention is completed. In between the time when you sign on to the study and the time when you complete the 6-month follow-up questionnaires, you will not be able to start a new treatment study for your NF1 or your pain; if you do, you would have to go off of this study at that time.

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

You have been diagnosed with NF1 and a plexiform neurofibroma and have chronic pain that you have indicated is interfering with your day to day activities.

**How many people will take part in this study?**

We expect 82 to 90 people with NF1 will participate in this study.

**Description of Research Study**

**What will happen if you take part in this research study?**

*Before you begin the study*

You were found eligible to participate in this study after you signed the screening consent, completed a history and physical exam, and answered specific questions about your pain, what you do to feel better, and medications you might be taking.

*During the study*

Once you sign this consent document, we will have our Registration Office 'randomize' you to one of the two groups:

1. Immediate ACT intervention group; or

2. The 'Wait-List' group.

You will be asked to complete ten questionnaires before starting the program. The questionnaires should take about 35 minutes to complete.

The questionnaires will collect information about the following areas:

1. Demographic questionnaire (basic information about demographic and educational history);
2. Pain interference, or how much pain interferes with your daily activities;
3. Quality of life (including energy level, appetite, mood, school attendance and how you get along with friends);
4. Chronic pain coping (how you cope with your pain);
5. Mood (including your enjoyment of life, problems sleeping, feelings of depression, anxiety);
6. Pain severity (how much pain you feel); and
7. Pain Management (what things you do now to cope with your pain)

We also will give you a 1- to 2-minute test of reading ability. In addition, everyone will have an electrocardiogram (ECG) to check heart rate, since heart rate is related to how we react to pain. This test is not painful. You will be asked to lie down and remain still for a few minutes and small sticky pads will be put on your chest. This test takes about 5 minutes. The Immediate Intervention group will get a total of two ECGs, and the Wait List group will get a total of 3 ECGs.

Also, if you have prior MRI scans of your plexiform tumor from an outside institution, we will ask you to have them sent to us for review, so that we can determine the exact location and, if multiple scans are available, whether there has been recent growth. However, this is an optional part of the study.

If you are in the 'Wait-List' group, you will return home for about two months. During this time, you will continue to manage your pain according to your doctor's recommendations.

If you are in the Immediate ACT group, you will participate in two 2-hour training sessions conducted over two days with an ACT trainer.

*ACT Training*

During the ACT training, we will teach you techniques for setting goals that reflect your personal values, and help you learn new ways of coping with pain. You will do practice exercises on your own between the 1st and 2nd sessions. At the end of the second session you will get a workbook with exercises to continue practicing at home. You will be encouraged to spend at least 10 minutes per day on these practice exercises.

When you are back home, you will receive weekly e-mails on different topics with a practice exercise each week. You also will be asked to join a biweekly Skype session with your trainer for about 30 minutes for each session.

*8 Week Follow up*

Everyone will be asked to return to NIH at about 8 weeks after starting the study. At this study visit, you will be asked to complete questionnaires again and have a second ECG. These questionnaires should take you about 35 minutes to complete.

If you are in the ACT group, you will return home and will be encouraged to continue using the ACT techniques practiced during the first 8 weeks.

Participants in the 'Wait-List' group will receive the ACT training consisting of two 2-hour sessions over two consecutive days, followed by the weekly e-mails and Skype sessions from home. After the 8-week ACT training, participants in the 'Wait-List' group will return to NIH to complete the questionnaires and ECG again.

Everyone will complete a final set of questionnaires from their home computer, tablet, or smartphone six months after the formal intervention ends.

That will be the end of your participation in this study. At this time, the study staff will be available to answer questions or can refer you to the appropriate health care provider if you need further assistance in managing the symptoms of NF1.

**Study Measures**

***Adult Background Information Form:*** This short questionnaire will ask for your gender, race, ethnicity, living situation, educational background and psychological history. It takes about 2 minutes to complete.

***Pain Interference Index:*** This 6 item questionnaire asks how pain has interfered with your life in the past two weeks. It takes about 2 minutes to complete.

***PROMIS Pain Interference Scale:*** This 8 item short questionnaire asks how pain affects things like sleep, mood and your activities. It takes about 2 minutes to complete.

***NF Quality of Life:*** This is a 19-item questionnaire asking about your day-to-day activities over the past month. Responses are selected from a 4-point scale based on how true the statement is ("Never" to "Almost Always") within the past month. This questionnaire will take about 5 minutes to complete.

***Pain related Anxiety (PASS):*** this is a 20-item questionnaire to assess pain-related anxiety in people with medical problems. Responses are rated on a 6 point scale from 'always' to 'never' to statements about pain and anxiety. It will take about 5 minutes to complete.

***Depression Scale (CES-D):*** is a 20-item questionnaire on which you are asked to rate how frequently in the past week you have experienced a list of symptoms, such as feeling depressed, enjoying life, having problems sleeping, and feeling liked by people. Items are scored on a 0 (rare or none of the time) to 3 (most of all of the time), and it takes about 5 minutes to complete.

***Pain Severity:*** You will be asked to rate your level of current and recent pain based on a 0 to 100 scale. Completing these items takes less than 1 minute.

***Chronic Pain Acceptance Questionnaire:*** This is a 20-item questionnaire that assesses your acceptance of your pain using answers on a 0 (never true) to 4 (always true) rating scale. It takes about 5 minutes to complete this questionnaire.

***Psychological Inflexibility in Pain Scale (PIPS):*** This is a 12-item questionnaire that assesses how you think about your pain. The questions are answered as 1 (never true) to 7 (always true). It takes about 3 minutes to complete.

***Pain Management Assessment:*** This questionnaire asks you about what things you have been doing to manage your pain, including things like relaxation, and medication. This measure takes 2 minutes to complete.

***ACT Inventory:*** This questionnaire asks how often you have completed the ACT strategies after participating in the ACT workshop. This questionnaire takes about 2 minutes to complete and will only be given at time points after you complete the ACT training.

***Patient Global Impression of Change (PGIC):*** This is a one-item question asked at the end of the study to get your impression of how much you have changed compared to how you were before starting. It takes less than 1 minute to complete.

***Word Reading Test:*** This short test of 1-2 minutes will give us information about reading ability and will be given at one time point only (typically at baseline).

**Study Chart**

| Procedure | Week 1 | Week 8 | Week 16 | Week 32 | Week 40 |
|---|---|---|---|---|---|
| Background Information Form | X | | | | |
| Pain Interference Index | X | | | | |
| Questionnaires | | | | | |
| • ACT group | X | X | | X | |
| • 'Wait-List' group | X | X | X | | X |
| ECG | | | | | |
| • ACT group | X | X | | | |
| • 'Wait-List' group | X | X | X | | |
| ACT Intervention | | | | | |
| • ACT group | X | | | | |
| • 'Wait-List' group | | X | | | |

If your score on the Depression measure is very high, the Principal Investigator or an Associate Investigator will speak to you about this and will make sure it is appropriate for you to enroll on the study. We also could refer you for any services you may need, if deemed appropriate.

**Risks or Discomforts of Participation**

**What side effects or risks can I expect from being in this study?**

The time commitment for the workshop attendance and completion of the questionnaires is the primary burden of participation.

**Potential Benefits of Participation**

**Are there benefits to taking part in this study?**

The aim of this study is to see if ACT works at helping individuals with NF1 cope with chronic pain. We do not know if you will receive direct benefit for participation in this study. However, you may experience an improvement in your ability to cope with your pain and in your overall quality of life. Also, we hope the information from this study will help us learn more about methods to help people with NF1 cope with chronic pain.

## Compensation

We will be providing you with $30, via direct deposit or check, each time you complete a set of questionnaires to thank you for your time.

## Alternative Approaches or Treatments

### What other choices do I have if I do not take part in this study?

You have the option to not participate in this study. You may still participate in any other support therapies offered by NIH. If you choose not to participate, it will not affect your medical care or participation in any other research study at NIH.

## Stopping Participation

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study investigator first.

## Research Subject's Rights

### What are the costs of taking part in this study?

There are no extra costs for being in this study. The study will provide the standard government reimbursement for travel costs, and external grant funding will cover additional travel and meal costs not covered by the government.

### Will your medical information be kept private?

We will do our best to make sure that the personal information you provide will be kept private. However, we cannot guarantee total privacy. Your questionnaires will be kept in locked file cabinets in the investigators locked office and your personal identifiable information will be stored in a password protected database that only the research team can access.

- The National Cancer Institute (NCI) and other government agencies which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

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 website, will include a summary of the results. You can search this Web site at any time.

## Certificate of Confidentiality

To help us protect your privacy, we have obtained a Certificate of Confidentiality. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

You should also know that there are several circumstances in which the Certificate does not provide coverage. These include when information:

- will be used for auditing or program evaluation internally by the NIH; or
- must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA).
- is necessary for your medical treatment and you have consented to this disclosure;
- is for other research.

In addition, identifiable, sensitive information protected by this Certificate cannot be admissible as evidence or used for any purpose in any action, suit, or proceeding without your consent.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

## Use of Data for Future Research

To advance science, it is helpful for researchers to share information they get from studying human data. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use data stored in scientific databases to advance science and learn about health and disease.
We plan to keep some of your data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your data will be used for research purposes only and will not benefit you. It is also possible that the stored data may never be used. Results of research done on your data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored data used for future research, please contact us in writing and let us know that you do not want us to use your data. Then any data that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete data once they have been shared with other researchers.

## OTHER PERTINENT INFORMATION

**1. Confidentiality.** When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

**2. Policy Regarding Research-Related Injuries.** The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

**3. Payments.** The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

**4. Problems or Questions.** If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Staci Martin Peron Ph.D., Building 82, Room 107, Telephone: 240-760-6025; or Pam Wolters, Ph.D. at 240-760-6035; or Brigitte Widemann, MD at 240-760-6203. You may also call the Clinical Center Patient Representative at 301-496-2626. If you have any questions about the use of your data for future research studies, you may also contact the Office of the Clinical Director, Telephone: 240-760-6070.

**5. Consent Document.** Please keep a copy of this document in case you want to read it again.

**COMPLETE APPROPRIATE ITEM(S) BELOW:**

**A. Adult Patient's Consent**

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/ Legal Representative _____ Date _____

Print Name _____

**B. Parent's Permission for Minor Patient.**

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/ Guardian _____ Date _____

Print Name _____

**C. Child's Verbal Assent (If Applicable)**

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

**THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM MARCH 13, 2019 THROUGH MARCH 28, 2020.**

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____