Impact of Nuedexta on Bulbar Physiology and Function in ALS

NCT03883581

Informed Consent Form

RESEARCH SUBJECT INFORMATION AND CONSENT FORM	
TITLE:	Impact of Nuedexta on Bulbar Physiology and Function in ALS

This consent form contains important information to help you decide whether to participate in a research study.

The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about and discuss with family or friends.

- **Being in a study is voluntary – <u>your choice</u>.**
- **If you join this study, you can still <u>stop at any time</u>.**
- **<u>No</u> one can <u>promise</u> that a study will help you.**
- **Do not join this study unless all of your <u>questions</u> are <u>answered</u>.**

After reading and discussing the information in this consent form you should know:

1. Why this research study is being done;
2. What will happen during the study;
3. Any possible benefits to you;
4. The possible risks to you;
5. Other options you could choose instead of being in this study;
6. How your personal health information will be treated during the study and after the study is over;
7. Whether being in this study could involve any cost to you; and
8. What to do if you have problems or questions about this study.

<u>Please read this consent form carefully.</u>

RESEARCH SUBJECT CONSENT FORM

Title:	Impact of Nuedexta on Bulbar Physiology and Function in ALS
Protocol No.:	None WIRB® Protocol #20190853
Sponsor:	ALS Association Clinical Management Grant
Investigator:	Lauren Tabor-Gray, PhD 4725 N. Federal Highway Fort Lauderdale, FL 33308 USA
Daytime Phone Number:	954 542 3429
24-hour Phone Number:	443 536 1234

Initial Concise Summary

Introduction

You are invited to participate as a volunteer in this clinical research study, which is funded by the ALS Association. Your participation in the study is voluntary. You have the right to decide whether or not to participate in this study without penalty. If you decide to participate in this study, you can withdraw at any time without penalty. During the study, you will be informed of any new information on the study drug that might affect whether you want to continue participating in the study. The study doctors or a designated study staff member can decide to withdraw you from this study, without your consent, if they judge that it would be better for your health. You could also be withdrawn from this study if you do not follow the instructions given to you or for other reasons as well. If you are withdrawn from the study by the principal investigator or study staff, the reason for your withdrawal will be explained to you. At the time of your withdrawal from the study, you may be asked to undergo additional tests for your safety.

In total, there will be approximately thirty (30) volunteers with amyotrophic lateral sclerosis (ALS) participating in this study.

This INFORMATION AND CONSENT FORM is intended to give you an overview of this clinical research study and what it involves. It may contain words that you do not understand. Please ask the principal investigator or a member of the study staff to explain any words or information that you do not understand. If you decide to participate in this study, you will be asked to sign and date this INFORMATION AND CONSENT FORM. This will confirm that you have been informed of the nature of the study and what it involves. Signing of this INFORMATION AND CONSENT FORM does not take away any of your legal rights. You will be given a copy of the INFORMATION AND CONSENT FORM after you have signed and dated it. During the study, if there is any

new information on the study drug, you will be notified and provided an amendment to the INFORMATION AND CONSENT FORM for your signature.

Information about the Research

Speech and swallowing difficulties occur throughout disease progression in individuals with ALS, who rate these symptoms as the worst aspect of the disease (Hillel and Miller, 1989). These impairments lead to social isolation and withdrawal, reduced quality of life and mental wellbeing, malnutrition, and aspiration pneumonia. A current gap in the clinical care of individuals with ALS is effective treatments to either improve or maintain speech and swallowing function. A promising drug is already approved by the FDA for use in ALS patients, Nuedexta, was recently documented to improve patient-rated speech and swallowing function (Smith et al., 2016). While this is promising, no study has yet determined the impact this pharmacologic intervention has on objective clinical and physiologic outcomes of speech and swallowing in ALS patients. The primary goal of this proposal is to rigorously evaluate the impact of an investigational pharmacological treatment, Nuedexta, on swallowing physiology, airway protection and speech intelligibility in individuals with ALS. Outcomes of this work will provide valuable physiologic insight into a promising therapeutic and help to reduce current gaps in the clinical management of individuals with ALS.

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

How long will I be in this research?

We expect that your taking part in this research will last 30 days.

Why is this research being done?

Speech and swallowing difficulties occur throughout disease progression in individuals with Amyotrophic Lateral Sclerosis (ALS) who rate these symptoms as the worst aspects of the disease (Hillel and Miller, 1989). There are currently no effective treatments for speech and swallowing impairment in ALS. The purpose of this research is to determine if Nuedexta, an FDA approved and routinely prescribed medication, improves speech and swallowing functions in patients with ALS.

What happens to me if I agree to take part in this research?

If you decide to take part in this research study, the general procedures include returning to the Phil Smith ALS Clinic for two visits spaced one month apart. Each visit will take approximately 1.5 hours. The first visit will occur prior to you starting Nuedexta and the second visit will occur one month after your first Nuedexta dose. During the research study,

Nuedexta will be taken according to FDA approved dosage at one time per day for the first 7 days and then one time every 12 hours (two times per day) for the remaining 23 days of the study.

During each visit, you will undergo tests to look at your swallowing, speech and ability to cough doing standard clinical exams. You will also be asked to fill out surveys on your ability to swallow and communicate. You will complete the following tests:

Swallowing X-Ray Study: During the swallowing portion of examination we will take an X-ray of your swallowing, this is called a Videofluoroscopy and is like a movie x-ray of you swallowing foods and liquids. For this test you will be asked to sit comfortably in chair and swallow barium. Barium is a substance that allows us to see how food and liquids flow through your mouth, throat, and esophagus during x-ray. It is white to the naked eye, but appears black in the x-ray. Barium may be thin, liquid, nectar, honey, or paste consistencies. You cannot feel the x-ray while it is on and the total time that the x-ray machine will be on will be under three-minutes (although the test will take approximately ten-minutes).

Cough Testing: We will ask you to cough into special equipment to measure the maximum strength of your cough.

Tongue Pressure Examination: During the tongue examination, we will measure your tongue strength by testing your ability to apply pressure to an air-filled tongue bulb that will rest on the roof of your mouth.

Speech Testing: We will record your speech using a small headset microphone as you read sentences and a short passage aloud.

Patient-reported Surveys: You will be asked to complete four routinely administered patient surveys including:

1. *Center Neurological Study Bulbar Function Scale, CNS-BFS (Smith, 2011):* The CNS-BFS is a 21-item validated, patient-reported scale indexing degree of bulbar dysfunction in the domains of speech, salivation and swallowing. A copy of the CNS- BFS appears in Appendix A.
2. *Eating Assessment Tool-10 (Belafsky, 2008):*The EAT-10 is a 10-item validated self report scale indexing an individuals perceived level of swallowing impairment. Patients rate each of the 10 items on a 5 point ordinal scale (O=no impairment,4=severe impairment) with a total EAT-10 score ranging between 1 and 40. A copy of the EAT-10 appears in Appendix B.
3. *Communication Participation Item Bank-10, CPIB-10 (Baylor et al., 2013):* The CPIB-10 is a 10-item validated, patient-reported survey assessing communicative effectiveness across contexts ranging from 0 (ineffective) to 30 (effective). A copy of the CPIB-10 appears in Appendix C.
4. *ALS Functional Rating Scale-Revised, ALSFRS-R (Cedarbaum, 1999):* The ALSFRS-R is the validated, gold standard survey assessing ALS symptom and disease progression to determine disease severity ranging from 0 (severe disease symptomology) to 48 (no overt symptoms). A copy of the ALSFRS-R appears in Appendix D.

At the conclusion of the research study, we will review the results of the swallowing, cough, tongue and speech testing measurements and compare them to your first visit. You can continue taking the study drug after the study is completed.

Could being in this research hurt me?
Nuedexta has been demonstrated to be safe and well-tolerated in patients with ALS. However, the most important risks or discomforts that you may expect from taking part in this research include side effects of the medication such as diarrhea, dizziness, cough, vomiting, asthenia, swelling, urinary tract infection, influenza and gas pains. Possible discomforts and risks of the testing procedures include:

- The radiation exposure in this study is thought to be minor. However, the effects of radiation add up over your lifetime. Repeated exposures may increase your risk of injury or disease. When deciding to enter this study you should consider previous and future potential exposures. Examples would include x-rays taken for a broken bone or radiation therapy treatments for cancer. Exposure to radiation during pregnancy can cause birth defects in unborn fetuses. Pregnant women should not undergo barium swallow procedures.
- Barium will be the material used to help us see your swallow function and sometimes when testing is done the barium may enter your lungs during swallowing causing you to cough or feel some discomfort. While small amounts of barium ingested into the lungs does not pose a significant health risk, large amounts ingested over several days can lead to aspiration pneumonia, which is a bad respiratory infection. Therefore, we will stop the test if we see barium enter the airway on more than two swallows of liquid or food to prevent major health risk.

This study may include risks that are unknown at this time.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

Will being in this research benefit me?
The most important benefits that you may expect from taking part in this research include improvements in speech and swallowing functions. However, it is possible that you may not experience any improvement in speech or swallowing during the study period.

Your participation, however, has the potential to help us better understand the impact of Nuedexta on speech and swallowing functions in patients with ALS.

What are my responsibilities if I take part in this research?
If you take part in this research, you will be responsible to take the study drug, Nuedexta, daily as prescribed and promptly report any side effects to the investigator

Will it cost me money to take part in this research?
The study drug will be prescribed and billed through your insurance company as standard of care. You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with the study drug.

In some cases, insurance does 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.

What other choices do I have besides taking part in this research?
This research is not designed to diagnose or prevent any disease. Your alternative is to not take part in the research.

What happens to the information collected for this research?
Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The ALS Association
- The Phil Smith ALS Clinic research team
- Government agencies, such as the Food and Drug Administration
- The Institutional Review Board (IRB) that reviewed this research
- The University of Florida Research Team collaborating on this study

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

We protect your information from disclosure to others to the extent required by law. We cannot promise complete secrecy.

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.

Data or specimens collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

Who can answer my questions about this research?
If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at (800) 562-4789, help@wirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What if I am injured because of taking part in this research?
If you are injured or get sick because of being in this research, call the study doctor immediately. The study doctor will provide emergency medical treatment. Your insurance

may be billed for this treatment. No other payment is routinely available from the study doctor or sponsor.

Can I be removed from this research without my approval?
The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- If it appears to be medically harmful to you
- If you fail to follow directions for participating in the study
- If it is discovered that you do not meet the study requirements
- You are pregnant

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

What happens if I agree to be in this research, but I change my mind later?
You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled.

If you decide to withdraw your consent to participate in this study for any reason, please contact one of the research team members. They will tell you how to stop your participation safely.

Will I be paid for taking part in this research?
You will not be paid for taking part in this research.

Statement of Consent:
I have been informed about this study's purpose, procedures, possible benefits and risks. I have also been told alternatives to being in the study and how my protected health information will be collected, used, and shared with others. I have been given the opportunity to ask questions. My questions have all been answered satisfactorily. I agree to be in this research study. I have received a copy of this form.

I authorize the confidential consultation of the study data including data collected about me by the organizations. I also consent to video recordings of my swallowing during the swallowing exams.

Commitment

- I will attend all scheduled visits on time;
- I will give true information about my medical history;
- I will not participate in another clinical research study during this study beginning with the screening session until the end of the study;
- I will respect all study restrictions and follow all instructions given to me by the study staff;
- I will advise the study staff of any change in my medical condition, minor or major, during the study.

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

Printed Name and Signature of Study Subject	Date
Printed Name and Signature of person obtaining consent	Date

Attestation Statement

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered the subject's questions. The subject appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the possible risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. Will participating in this study cost you anything? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

_____	_____
Printed Name of Person Conducting the Informed Consent Discussion	Position
_____	
Signature of Person Conducting the Informed Consent Discussion	Date