RESOURCE GUIDE

SECTION 2 - ALS Research

EMORY
ALS CENTER *Celebrate Life... Imagine a Cure*

Research Team

Clinical trials are health-related studies in people that are closely supervised and carefully follow a pre-defined protocol. Each study answers scientific questions and tries to find better ways to prevent, screen for, diagnose or treat a disease. Clinical research studies involve people, but do not involve treatment with an experimental drug or testing of an experimental device. These studies may help doctors, researchers and scientists learn more about the disease, so that they may diagnose, prevent, treat or cure the disease. Our Research Team works with participants in both.

Research Update

Spring 2021

EMORY ALS CENTER *Celebrate Life... Imagine a Cure*

ALS research in the time of COVID has been different – but we are continuing to work toward understanding the causes and drivers of ALS. We at the Emory ALS Center continue to be actively engaged in research projects that range from basic questions about the causes of ALS to clinical trials of new drugs to treat people with ALS. Please read below to learn more about our research program and projects.

Though much of our "wet lab" research has been on hold since March, our extensive ALS database and biobank allows us to continue to ask questions about the clinical features of disease (i.e. age of onset, rapidity of progression) and how that relates to protein markers in the blood and the brain, and what relationship these measures have to a person's genetic makeup.

Some New Projects:

- In collaboration with investigators at the University of Massachusetts and the NIH, and funded by ALSA, Dr. Glass is working on generating a repository of whole genome sequences collected from ALS patients around the world. This will be a valuable collection of genetic information unprecedented in size and will be made available to any and all investigators who are studying any aspect of ALS.
- The Emory ALS Center has just been funded by the National Institutes of Health to investigate "Pathobiology Neurodegeneration in C9ORF72 Repeat Expansion". This project, in collaboration with investigators at the Mayo Clinic, Johns Hopkins, and the Massachusetts General Hospital will use animal models and human tissues to identify causative factors in patients with this form of genetic ALS.
- We are well into the clinical trials of gene therapies for ALS patients carrying either the SOD1 or C9ORF72 genetic mutation. Promising results have just been reported [link to NEJM press release] and we continue to test these extraordinary new therapies. New trials are being designed and will soon be initiated for other genetic targets, and even for the possibility of preventing disease.

Our Investigators:

Dr. Jonathan Glass, Director. Professor of Neurology and Pathology. Dr. Glass actively collaborates with other ALS investigators around the world on multiple projects examining ALS genetics, immunology, neuropathology, and animal and cellular models of ALS. Dr. Glass also continues his work on discovering biomarkers of ALS, which necessitates the participation of PALS and CALS. We are collecting blood and spinal fluid samples from patients for our research. Family members and non-related adults are also important participants in our studies, serving as "controls" that allow us to compare results between people living with and without ALS.

Dr. Christina Fournier, Associate Professor of Neurology. Dr. Fournier is well into her 5-year research grant from the Veterans Administration to develop a new questionnaire to measure the progression of ALS. The first phase of the project is complete with creation and validation of the Rasch-Built Overall ALS Disability Scale (ROADS), a new and improved tool for measuring the degree of disability in PALS. The ROADS is an improvement over the ALS Functional Rating Scale (ALSFRS-R), as it is shown to be more reliable and is expected to be more responsive in capturing smaller changes in disability. It is hoped that this new scale will improve the efficiency of future ALS clinical trials. You can read about ROADS and be directed to the ROADS webinar here. Many thanks to all the patients who helped by completing the questionnaire and then completing it again from home. We will now be using the ROADS along with the ALSFRS-R in our clinics to help us get a clear picture on how our patients are progressing. Additional opportunities to participate in this important research may be

available at your clinic visit. Please consider participating in this important effort, as these efforts help us to design better clinical trials in the future.

After 20+ years leading our research team, Meraida Polak, RN has transitioned into a part-time role as a clinical research nurse. We are pleased to announce that **Jane Bordeau, RN, who has been with us for over ten years, is our new Research Director.**

Ezana Assefa, PhD Student. Ezana is a new graduate student working with Dr. Glass on the question of why ALS patients are so different in their clinical characteristics. This is even true for those carrying a genetic form of the disease. Ezana has embarked on a project looking at genetic factors (i.e. genetic modifiers) that may underlie this disease heterogeneity using DNA and cells generated from skin biopsy samples from patients with genetic ALS, but with varying clinical features. Ezana is just getting started, but this promises to be an exciting project.

We at the Emory ALS Center understand the dire need for effective treatments for ALS. The only way to help develop new therapies for ALS is through rigorous scientific investigation. This type of investigation requires the efforts of teams of clinicians and scientists around the world, adequate research funding, and time.

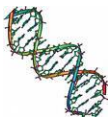
Most importantly, we need the partnership of our patients and their families to study and better understand their disease!

Visit our website to learn about upcoming clinical research and trials we are offering: www.als.emory.edu

Clinical Trial Opportunities: (treatment with an experimental drug)

Platform Trial in ALS: NOW ENROLLING—The Platform Trial is evaluating safety and efficacy of 5 different novel drug therapies in ALS. To learn more about this unique design in ALS treatment research, please visit https://www.massgeneral.org/neurology/als/research/platform-trial. For more information contact Arish Jamil at arish.jamil@emory.edu
Biogen C9orf Study: LIMITED ENROLLMENT-- The C9orf Study is evaluating the safety and potential efficacy of an investigational drug for people living with ALS caused by the C9orf gene mutation. All participants will receive either the investigational drug or placebo (inactive drug), and all study related visits and care, at no cost. Assistance with travel, accommodations, and reimbursement for study related expenses may be available. For more information contact Anna Partlow at 404-778- 3181 or anna.partlow@emory.edu.
Biogen Ataxin Study: NOW ENROLLING--This is a first-in-human gene therapy trial for sporadic ALS to evaluate the safety of BIIB-105. There will be 6 cohorts, with subjects being randomized 3:1 to receive active drug or placebo. Five doses of drug will be administered via lumbar puncture over 12 weeks, with total participation period to be approximately 29 weeks. For more information, please contact Annie Rowland at anne.rowland@emoryhealthcare.org
Mitsubishi Oral Drug Dosing Regimen Study: ENROLLING SOON-- The purpose of this study is to test if an oral formulation of the FDA-approved IV drug edaravone (Radicava) is effective and safe in patients with ALS, and to compare its effects when given in 2 different dose regimens. Subjects will be randomized 1:1 to either Group 1 which will receive active drug daily for 14 days, followed by 2 weeks off drug, or Group 2 which will receive edaravone to be taken daily in 28-day on/off cycles. For more information, please contact Virginia James at virginia.james@emory.edu

Clinical Research Opportunities: (no experimental drug treatment)

Research Study	Study Details	Contact Person
Clinical Research in ALS (CRiALS)  • To learn more about neurological disorders • To contribute to Project MinE	• For ALS patients, blood relatives and healthy unrelated volunteers • Procedures include donation of a blood sample, skin sample and/or spinal fluid and an information questionnaire	Arish Jamil 404-727-1273 Arish.jamil@emory.edu www.projectmine.com
Research Survey on ALS Genetic Testing-- Purpose is to understand the experiences of affected and at-risk individuals with ALS genetic testing- • (Collaboration with Srika Amin, grad student in Genetic Counseling)	• For English speaking adults with ALS who have been *offered* genetic testing and • Family members who have been *offered* genetic testing	Take online survey at the link below: EmoryALSGeneticCounselingSurvey
Pathogenesis in C9ALS (PICALS)	For patients with sporadic ALS, Patients with C9ALS, healthy blood relatives of people with C9ALS. Three visits over 12 months with the option of ongoing visits. Will have exams, questionnaires and donate blood and spinal fluid. • Relatives of people with C9 ALS will have free genetic counseling and testing to learn results.	Karon Simmons 404-712-4182 Kmsimm2@emory.edu
Microbiome in the progression of ALS (MPALS): RECRUITING • Microorganisims in the gut communicate with the brain and play a role in some conditions. • Does this play a role in the progressions of ALS?	• For ALS patients with live in spouse/partner or caregiver • Couples mail in saliva and stool samples three times over 6 months	Karon Simmons 404-712-4182 Kmsimm2@emory.edu

HAVE YOU ENROLLED IN THE NATIONAL ALS REGISTRY??

https://www.cdc.gov/als/Default.html

EMORY ALS CENTER Celebrate Life... Imagine a Cure

Is research right for me? Am I right for research?

By Meraida Polak, RN, BSN
Clinical Research Director, Emory ALS Center

While most everyone is interested in results of research seeking causes and treatments for ALS, not everyone has the opportunity to personally participate in the process. Progress can only be made with the generosity of patients and families that choose to participate. But research is not for everyone. If the opportunity to participate in a research project arises, here are some things for you to consider.

There are two types of research that seek participants:

1. Research that follows patients as they progress through the illness: This might include: surveys, observations over time and/or collection of blood, spinal fluid or tissue. This type of research may provide no benefit to the participant other then the satisfaction of knowing that they helped move science forward. This may include a simple one-time donation of blood, or having blood and spinal fluid taken several times/year, or the donation of your tissue through autopsy after death.

2. Research with experimental treatment: This might be a dietary plan, a pill, an injection, an infusion, an implant or a transplant. Treatment studies are divided into phases. Phase I studies seek to evaluate whether the treatment is harmful and if so, the treatment is abandoned. Phase II seeks to identify a hint that the treatment might work while testing to see what the best dose might be. Phase III determines if the treatment is effective. Phase IV studies are done after the drug or treatment has been approved and marketed. The purpose is to to gather information on the drug's effect in various populations and any side effects associated with long-term use. Most investigational new drug studies include a group of participants who are assigned to a placebo (sugar pill) group for all or part of the study. Neither the participant nor the physician/study team know if the patient is taking a placebo or the actual drug. Some placebo controlled studies will offer participants the opportunity to get active drug after the blinded phase has ended.

Is it for me? Ask yourself:
How will I feel if my participation does not help me personally? Is it enough to know that I am helping others?

Am I prepared to accept risk and if so, how will I feel if I am harmed by my participation? All research poses a risk. Even a single donation of blood could result in bruising or discomfort. Experimental treatments have risks small and large up to even causing paralysis or death. And there are risks that no one even knows about yet! It is this participation where the risks are first identified.

Will I feel like a "guinea pig?" The term guinea pig is a derogatory term for test subject that implies exploitation. Research participants are indeed test subjects but the relationship between the investigators and the participants is one of a partnership with both parties sharing a common goal. If you feel like you would be

exploited or taken advantage of then research might not be for you. It might go back to the first question, is it enough to know that you are helping others.

Do I clearly understand what I am signing up for? One of the most important responsibilities of the research team is to make sure that you have all of the information that you need to make an informed, educated

decision about joining the research or not. You should always feel free to volunteer or not and always feel free to change your mind and withdraw if you want to.

Research studies are NOT designed to help the participants. They are designed to answer a question, such as, "does this pill work to slow down ALS." Are you OK with that?

Am I right for research?
Every study has two sets of requirements. First are the eligibility requirements. When you are learning about the study, you will be able to evaluate yourself and get an idea if you meet the entry requirements. If you think that you might meet the criteria, the research team will determine if you meet the requirements. This might be decided after a casual conversation and review of your records. Or it might be determined after you have volunteered and have been screened for the study. But if you know that you don't qualify, then inform the research team. People who are comfortable being honest with the researchers are right for research.

Second are requirements to do specific things during the ongoing study. This means coming to all your appointments on time, taking the therapy as directed, and keeping a diary or log of how you are doing. Some studies require frequent visits. Others require fewer visits but more diary keeping on how you are tolerating the treatment. People who can get to the clinic and take their medications and keep everything written down are right for research.

One of the most important responsibilities for the investigator is the process of informed consent. This begins with completely informing the potential participant of the study goals, risks, possible benefits, and responsibilities. No research is allowed to take place until the participant has signed a form giving permission. If you consider becoming a research participant, you will be given a written form with enough time to read every word and consider every aspect. You should note your questions or any aspect of the project that you are not crystal clear about.

We all want to know the cause of ALS and we desperately want to find the cure. This cannot be done without people with ALS participating in the research process. But research is not for everyone, and if it is not right for you, there are other ways of helping that may be just as important.