HEALEY ALS Platform Trial

Weekly Q&A – March 30, 2023

Patient Navigation
Central resource for people living with ALS

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Weekly webinar registration:

https://bit.ly/3r6Nd2L

ALS Link sign-up:

https://bit.ly/3o2Ds3m

Upcoming Webinars:

April 6th- Weekly Q&A

April 13th- Weekly Q&A

April 20th- Weekly Q&A

On the Importance of Biomarkers in ALS

"I thought the last two webinars were fantastic! The guest speakers were great at explaining the science. I feel like we are closer to getting the right cocktail to help stop and reverse symptoms. Thank you for hosting the weekly webinars. They provide hope for everyone!"

Weekly & Monthly Updates: 2023

March 23, 2023: Weekly Q&A with guest speaker Jeffrey Rothstein, MD, PhD

Sabrina Paganoni, MD, PhD of Massachusetts General Hospital presented this week's updates on the HEALEY ALS Platform Trial and answered questions from the audience. We were joined by guest speaker Jeffrey Rothstein, MD, PhD, Director of the Robert Packard Center for ALS at Johns Hopkins University, to discuss the importance of identifying biomarkers in ALS, recent research findings related to TDP-43, and future directions in ALS research.

Watch recording|Download slides (PDF)

March 16, 2023: Weekly Q&A with guest speaker Nicholas Maragakis, MD

Sabrina Paganoni, MD, PhD of Massachusetts General Hospital presented this week's updates on the HEALEY ALS Platform Trial and answered questions from the audience. We were joined by guest speaker Nicholas Maragakis, MD of Johns Hopkins Medicine to discuss recent research findings related to TDP-43, and the pivotal importance of exploratory biomarkers in ALS research.

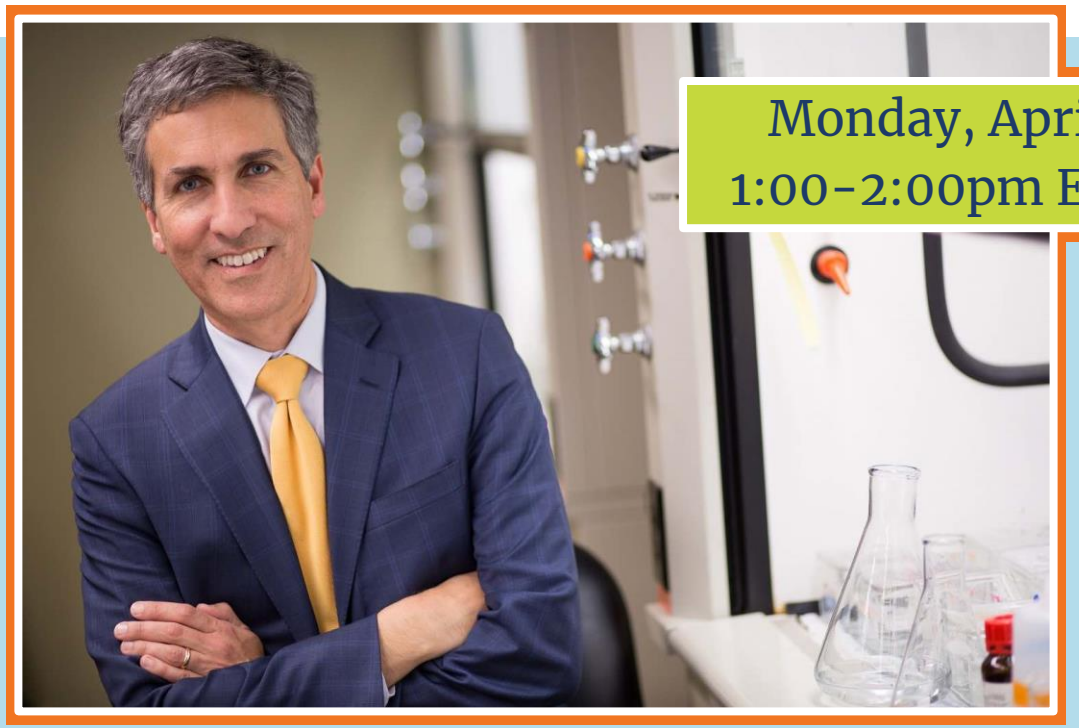
Watch recording|Download slides (PDF)

View Recordings:

https://bit.ly/3g4kzfv

The ALS Association/Northeast ALS Consortium Educational Webinar

Why lumbar puncture and CSF biomarkers are important to ALS therapeutic development



Monday, April 17th
1:00-2:00pm Eastern

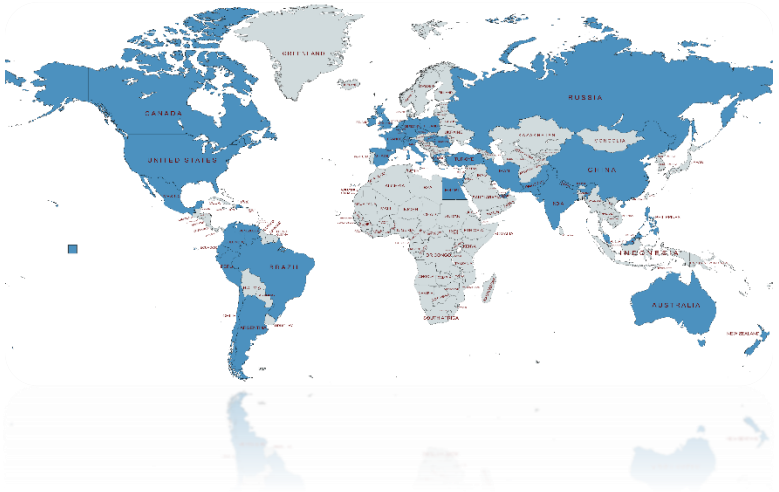
Presenter: Nicholas J. Maragakis, M.D., Johns Hopkins University

Register Here:

https://bit.ly/3JTZqzN

Recording will later be available under "educational webinars" on neals.org

Building Community & Partnership in ALS Research



Patient Navigator: Central Resource

2,602 Total emails/phone calls/zoom calls with ALS families
630 Uses of the Online Eligibility Checking Tool
39 Countries in contact about research

Weekly Webinars: News & Updates

115 Public Q&A webinars hosted to date
50+ Guest speakers featured
8,317 Total attendees, **71** Weekly average
40,553 Total views on YouTube

Drug Science Q&A Webinars

6 Webinars hosted (Regimens A,B,C,D,E,F)
8,481 Total views on YouTube
242 Questions answered live

(Data Collected Oct 2020-Mar 2023)

Recent News! Updates on Regimen F

Regimen F Drug Science Q&A Webinar

Hosted: Monday, March 27th at 5-6 PM Eastern Time

Recording Coming Soon!

https://bit.ly/3r6Nd2L

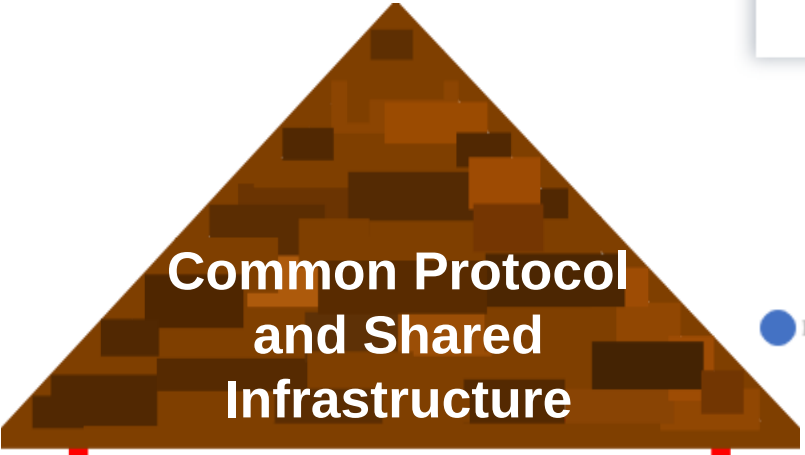
First participant enrolls in Regimen F!

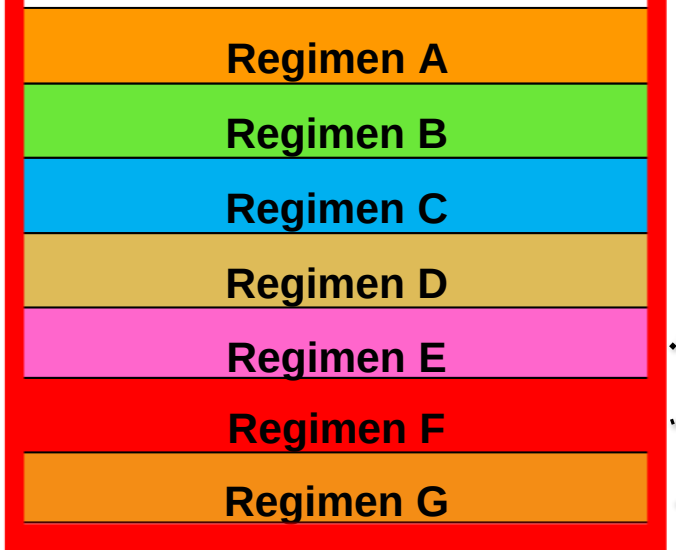
View Press Release: https://bit.ly/3LYNMXd

Thank You

This breakthrough trial would not be possible without your participation

HEALEY ALS Platform Trial:



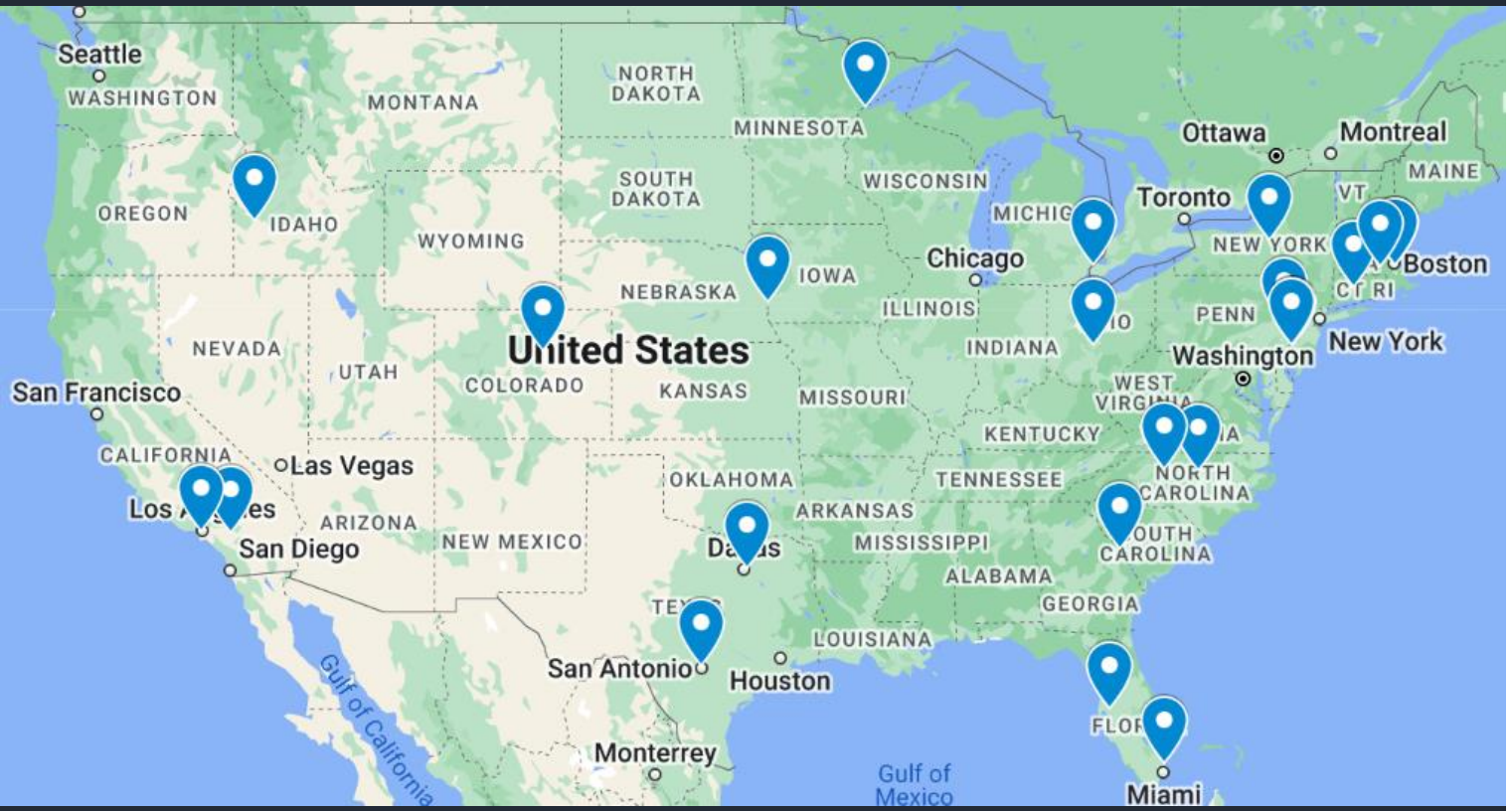


SEELOS THERAPEUTICS | ENROLLMENT COMPLETE

Calico | IN START-UP

DENALI THERAPEUTICS | IN START-UP

23 Sites Currently Active for Regimen F



(as of 3/30/23)

- Nova Southeastern University
- Essentia Health
- Texas Neurology
- Mass General Hospital
- University of Nebraska
- Hospital for Special Care
- Henry Ford Hospital
- Augusta University
- Beth Israel Deaconess
- University of Texas HSC
- University of Colorado
- Loma Linda University
- Ohio State University
- Cedars Sinai Medical Center
- Duke University
- Wake Forest University
- Saint Alphonsus
- UMass Worcester
- Lehigh Valley
- Thomas Jefferson
- University of South Florida
- University of Pennsylvania
- SUNY Upstate

Site Map & Contacts:

https://bit.ly/3g2NZr5

Regimen F Resources on MGH Website

Regimen F: ABBV-CLS-7262, by Calico and AbbVie- Now Recruiting

ABBV-CLS-7262 is an investigational drug developed by Calico Life Sciences LLC in collaboration with AbbVie Inc. ABBV-CLS-7262 aims to restore function in cells affected by ALS by normalizing protein synthesis and preventing further sequestration and aggregation of TDP-43, thereby protecting neurons, and possibly slowing ALS progression.

The integrated stress response (ISR) is a fundamental transient process that regulates cell function during various stressful conditions. Tissue studies suggest that the ISR is chronically induced in people with ALS. It is proposed that TDP-43 aggregates, a hallmark feature in the motor neurons of people with ALS, could be formed by a chronically induced ISR. ABBV-CLS-7262 activates the protein complex eIF2B, which is a key regulator of the ISR. Binding of ABBV-CLS-7262 desensitizes eIF2B to stress and decreases the ISR. Reduction of the ISR restores normal protein synthesis, reduces TDP-43 sequestration in stress granules, and may decrease TDP-43 aggregation.

A prior first-in-human study of ABBV-CLS-7262 showed that this drug was well-tolerated by participants, demonstrated target engagement by increasing eIF2B enzymatic activity, and suppressed the ISR in blood cells. ABBV-CLS-7262 crossed the blood brain barrier at concentrations predicted to be efficacious in ALS. ABBV-CLS-7262 is currently being investigated in a Phase 1b study in people with ALS (NCT04948645), and will be studied further as part of the HEALEY ALS Platform Trial.

Watch this video for more information on the mechanism of action behind ABBV-CLS-7262.

Download brochure

Healey Center
Sean M. Healey & AMG Center for ALS at Mass General

NEALS Northeast Amyotrophic Lateral Sclerosis Consortium

HEALEY ALS Platform Trial

Regimen F

ABBV-CLS-7262

Developed by Calico Life Sciences LLC in collaboration with AbbVie Inc.

Investigational products included in the HEALEY ALS Platform Trial are selected by a team of experts after careful review of the study drug and the science supporting its treatment potential in Amyotrophic Lateral Sclerosis (ALS). Regimen F is testing an experimental medication called ABBV-CLS-7262, and the trial will involve in-person study visits every 4 to 8 weeks (about 6 visits total over the course of 24 weeks).

Please discuss the possible benefits and risks of this investigational product with your study team.

Visit our website to learn more about what to expect in the trial process:
https://bit.ly/3ExRal8

About Regimen F:

Regimen F is a Phase 2/3 trial enrolling approximately 240 participants to evaluate the safety and efficacy of ABBV-CLS-7262 as a potential treatment for ALS. This regimen involves biomarker analysis and cerebrospinal fluid collection via lumbar punctures to assess the effects of ABBV-CLS-7262.

3:1 Active Drug to Placebo Ratio: Participants who enroll in this trial have a 3 in 4 (75%) chance of being assigned to active study drug and a 1 in 4 (25%) chance of being assigned to placebo during the initial 24-week randomized controlled trial (RCT) period.

Active Treatment Extension (ATE): Participants have the option to enroll in the ATE for ABBV-CLS-7262 upon completion of the 24-week RCT. During ATE, all participants will receive the active study drug.

To see if you may qualify, please review the list of eligibility criteria:
https://bit.ly/30ctynm

For general questions about the HEALEY ALS Platform Trial, **Contact the Patient Navigator:**

healeyalsplatform@mgh.harvard.edu
833-425-8257 (HALT ALS)

https://bit.ly/3SIwH4X

Printable Brochures!

↓

Regimen F Brochure

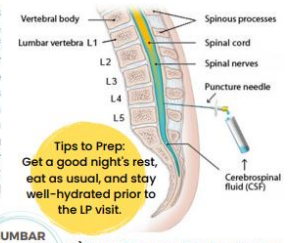
Lumbar Puncture Brochure

General Platform Trial Brochure

Understanding HEALEY ALS Platform Trial Study Procedures

LUMBAR PUNCTURE

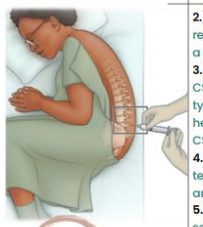
A Lumbar Puncture (LP), or Spinal Tap, is a procedure to remove a small sample (10-15mL or ~1 tablespoon) of cerebrospinal fluid (CSF) from the lower spine. CSF is the fluid that surrounds the brain and spinal cord, and it contains proteins, cells, and other substances that may be important biomarkers in ALS research. During the procedure, a needle is inserted between two lumbar vertebrae (backbones) in the lower back and into the space in the spinal canal that contains CSF.



Tips to Prep: Get a good night's rest, eat as usual, and stay well-hydrated prior to the LP visit.

Sometimes, people feel worried that a lumbar puncture could be risky or painful. In reality, this is a safe and common procedure to collect CSF!

LUMBAR PUNCTURE STEP BY STEP



1.) You will be asked to sit or lie down in a position that helps widen the spaces between the bones of the lower spine.

2.) The doctor will cleanse the skin on your lower back to reduce risk of infection, then use a small needle to inject a local anesthetic (such as lidocaine) to numb the site.

3.) The LP needle is inserted into the space containing CSF. A special atraumatic spinal needle (Sprotte) is typically used to reduce the chance of a post-puncture headache. The doctor may need to readjust the needle if CSF cannot be drawn with the first insertion.

4.) Spinal fluid is collected into specimen tubes for lab testing. The LP needle is removed, your back is cleaned, and a band-aid is placed over the LP site.

5.) For your comfort and safety, it is recommended that someone drive you to and from the LP study visit.

QUESTIONS? Prior to enrolling in a clinical trial, your study team will discuss the LP procedure with you. Please ask your study team for clarification if you have any questions while reviewing the informed consent form.

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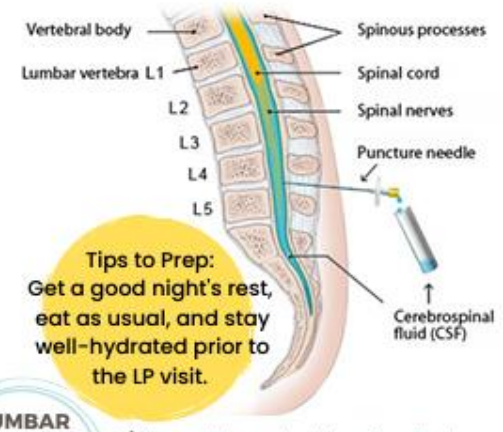

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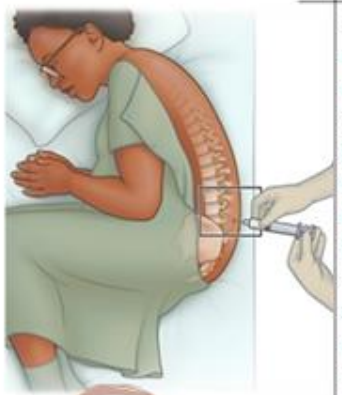

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Lumbar Puncture Information Sheet

COMMON QUESTIONS

Q: How long does a LP take?

A: The procedure typically takes 20-30 minutes, with an additional 30-60 minute rest period after the LP. The body can replenish 10-15mL of CSF in about an hour.

Q: Does it hurt? What are the risks?

A: You may experience pressure when the needle is inserted. There may be very brief leg pain if the needle touches a nerve ending that floats at the base of the spine. The needle is inserted well below the spinal cord, so there is no risk of paralysis.

Q: Why do we do LPs in ALS research?

A: Spinal fluid from LPs is critical to move science forward in ALS. Motor neurons live in the brain and spinal cord, constantly bathing in cerebrospinal fluid, so CSF is one of the most powerful ways to get direct information about the nervous system.

Q: What information do we get from CSF?

A: CSF is important to measure the effects of an investigational drug in a clinical trial. It also provides protein and other markers to predict and track disease progression, and helps identify subsets of people who best respond to a specific study drug.

AFTERCARE TO-DO'S

As you leave your study visit and head home, it is important to remember a few things to ensure your health and safety.

- Stay well-hydrated. Drink plenty of water (6 glasses of fluid in the 12 hours after your LP). This will help your body replace the fluid removed during the procedure and reduce the likelihood of getting a post-LP headache.
- Rest & Relax. Avoid strenuous physical activity for the rest of the day. Laying flat will help reduce the possibility of developing a headache.
- Continue with your usual diet.
- Several hours after the LP, you may remove the band aid and shower as you wish. Your study team can answer any questions about timing.
- If no complications occur and you are feeling well, you may return to your normal activities the next day.

SYMPTOM MANAGEMENT

Headache:

- About 30% of people experience a post-LP headache. If you notice a mild headache, hydration and lying flat can help. Drinking a beverage with caffeine (in addition to water) may also help, as well as over-the-counter Tylenol (follow dosage instructions on the bottle).
- If your headache becomes more than mild or persists longer than 24 hours, and is not relieved by the above interventions OR if you develop a fever at any time following the LP, please contact your study team right away.

Back Discomfort:

- If you experience back discomfort, try applying ice wrapped in a towel to the affected area for 20 minutes, 3-4 times over the course of the day.

Guest Speaker

James Berry, MD MPH

Director, Mass General Hospital Multidisciplinary ALS Clinic
and Neurological Clinical Research Institute (NCRI)