Thank you for joining the weekly webinar!
We are admitting audience members from the waiting room.
Please allow a few moments for the webinar to begin.
HEALEY ALS Platform Trial

Weekly Q&A – May 4, 2023
HEALEY ALS Platform Trial:

Common Protocol and Shared Infrastructure

Regimen A
Regimen B
Regimen C
Regimen D
Regimen E
Regimen F
Regimen G

Screen for eligibility → Randomization 3:1 → Active

Active

ENROLLMENT COMPLETE

ENROLLING

IN START-UP
46 Sites Currently Active for Regimen F

(as of 5/4/23)

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
University of Iowa
California Pacific Med Center
Houston Methodist
Vanderbilt University
University of Minnesota
Washington University
Barrow Neurological Institute

University of Miami
Temple University
University of Virginia
Johns Hopkins University
University of Southern CA
Holy Cross Hospital
University of Washington
University of Utah
Penn State Hershey
University of Michigan
University of Kansas
Stony Brook University
University of Cincinnati
Mayo Clinic Rochester
Northwestern University
Georgetown University

Site Map & Contacts:
https://bit.ly/3g2NZr5
Checking Site Status Online

List of Participating Sites

Many sites are expected to start enrolling for Regimen F soon. Sites marked “Recruiting” are currently enrolling participants.

Sites marked "Active, Not recruiting" are active in the Platform Trial (for example, they are following participants in ongoing regimens that have already completed enrollment) but are not enrolling new participants at this time.

<table>
<thead>
<tr>
<th>Site</th>
<th>State</th>
<th>Enrollment Status</th>
<th>Trial Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo Clinic Florida</td>
<td>FL</td>
<td>Active, Not recruiting</td>
<td>Jany Poulitt</td>
</tr>
<tr>
<td>Nova Southeastern University</td>
<td>FL</td>
<td>Recruiting</td>
<td>Donovan Mott</td>
</tr>
</tbody>
</table>

Contact a study team near you to discuss enrollment opportunities

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 elf2B, which is a key regulator of the ISR. Binding of ABBV-CLS-7262 desensitizes elf2B 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 elf2B 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 HEALY ALS Platform Trial.

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

Download brochure

Regimen F Drug Science and Mechanism of Action

Topic: Regimen F Drug Science and Mechanism of Action

Recording Available: https://bit.ly/3mQy5qQ

ABBV-CLS-7262 is ready to be evaluated as a new potential treatment for ALS

Problem

- IDR is activated in ALS
- Aggregates of the protein TDP-43 are observed in most ALS cases
- Drugs tested in ALS clinical trials must have their intended biological effect in people
- The right dose needs to be administered in clinical trials
- Our understanding of ALS is incomplete

Calico

- ABBV-CLS-7262 is a potent inhibitor of the ISR by binding to, and activating, eIF2B
- ABBV-CLS-7262 dissolves stress granules containing TDP-43 which may reduce formation of new TDP-43 aggregates
- Blood cells from people given ABBV-CLS-7262 show increased eIF2B activity and reduced ISR
- ABBV-CLS-7262 was measured in the CSF at levels predicted to be pharmacologically active at tolerated doses
- CSF and blood samples will improve our understanding of the ISR in ALS and may identify people most likely to respond to ABBV-CLS-7262
The ALS Association/Northeast ALS Consortium Educational Webinar

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

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

Monday, May 8th 1:00–2:00pm Eastern

Register Here:

https://bit.ly/3JTZqzN

Recording will later be available under “educational webinars” on neals.org
Patient Navigation
Central resource for people living with ALS

Phone: 833-425-8257 (HALT ALS)
E-mail: healeyalsplatform@mgh.harvard.edu

Weekly webinar registration:
https://bit.ly/3r6Nd2L

ALS Link sign-up:
https://bit.ly/3o2Ds3m

Upcoming Webinars:
May 11th- Weekly Q&A
May 18th- Weekly Q&A
May 25th- Weekly Q&A