HEALEY ALS Platform Trial

Weekly Q&A – Oct 27, 2022

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

[Logos and images from various organizations and sponsors related to ALS and neurology]
The 1st Ever ALS Platform Trial

Video Link:
https://www.youtube.com/watch?v=AkUVl-KsUfU

The goal of the HEALEY ALS Platform Trial is to screen drugs rapidly and efficiently, get solid answers, and determine next steps.
The Platform Trial is Governed by a Master Protocol, a Common Protocol for Multiple Regimens
Common Protocol – Schema for Each Regimen

Screening Period

- ~160 Randomized
  - 3:1

Treatment Period = 6 Months*

- ~120 Participants on Active
- ~40 Participants on Placebo

* Randomized Placebo-Controlled Treatment Period followed by Open Label Extension
Common Protocol – Endpoints

**Primary Endpoint**
- Change in disease severity through 24 weeks
- ALS Functional Rating Scale-Revised (ALSFRS-R) + Mortality
- Potential to provide confirmatory evidence with overall type I error of 5%

**Secondary Endpoints**
1. Change in respiratory function - slow vital capacity (SVC)
2. Change in muscle strength - hand held dynamometry (HHD)
3. Survival

**Safety Endpoints**

**Biomarkers and Exploratory Endpoints** (DNA, NfL, Speech app, Home Spirometry)
Assessing emerging biomarkers/outcome measures

**DNA** – genetic analysis in progress for all regimens

**Neurofilaments** – NfL analysis in progress for all regimens

**Biomarkers** (Blood, Urine, CSF) – several drug-specific and MOA biomarkers are being analyzed in each regimen

**Speech Analysis** – data collected for regimens A-D; results expected in the coming months

**Home Spirometry** – critical during the pandemic for regimens A-D

Additional biomarkers/outcome measures being considered for upcoming regimens (PBMCs, ROADS)
Weekly Recordings Available on Website

Visit the Website: https://bit.ly/3g4kzfv

Webinar Recordings

Science & Mechanism of Action Series

Weekly & Monthly Updates

October 6, 2022: Weekly Q&A featuring discussion of Regimen C/CNM-Au8 results
Merit Cudkowicz, MD, MSc and Sabrina Paganoni, MD, PhD presented this week’s updates on the HEALEY ALS Platform Trial and answered questions from the audience. We were joined by the co-lead investigators for Regimen C and representatives from Clene Nanomedicine, Inc. to discuss the trial results for CNM-Au8.
[Watch recording.]

September 29, 2022: Weekly Q&A featuring discussion of Regimen B/Verdiperstat results
Merit Cudkowicz, MD, MSc and Sabrina Paganoni, MD, PhD presented this week’s updates on the HEALEY ALS Platform Trial and answered questions from the audience. We were joined by the co-lead investigators for Regimen B and representatives from Biohaven Pharmaceuticals to discuss the trial results for Verdiperstat.
[Watch recording.]
HEALEY ALS Platform Trial

Ongoing and Upcoming Regimens

Regimens D: ongoing

Regimen E enrolling new participants now

Additional Regimens in start-up or selected
Regimen E
TREHALOSE (SLS-005)

- Trehalose is a disaccharide composed of 2 glucose molecules
- Humans do not make trehalose, but can metabolize it
- Oral trehalose is not absorbed due to breakdown by gut trehalases (<0.5%)
- Therefore, it is administered IV to bypass the gut trehalase enzymes
- Trehalose penetrates muscle and brain
- When tested in vivo, treatment with trehalose resulted in preservation of motor neurons in the ventral horn of the spinal cord, improved muscle strength, and prolonged survival in SOD1 mouse models of ALS

2. Zhang et al, 2014
3. Li et al, 2015
The ALS Association/Northeast ALS Consortium Educational Webinar

Update on Healey ALS Platform Trial Regimen E: Trehalose for ALS

UPDATE ON REGIMEN E
TREHALOSE FOR ALS

Merit Cudkowicz, MD, MSc
SEAN M. HEALEY & AMG CENTER FOR ALS AT MCH

Shafeeq Ladha, MD
BARRON NEUROLOGICAL INSTITUTE

TUESDAY 4 OCTOBER 3 PM EDT

Recording Available!


Recording available under “educational webinars” on neals.org
Enrollment Updates (as of Oct 27, 2022)

- 158 individuals have signed informed consent
- 116 individuals have been randomized within Regimen E

Thank You

This breakthrough trial would not be possible without your participation.

Your partnership in research is what keeps us filled with passion, dedication, and the commitment to uncover new promising treatments for ALS.

Every research participant, whether on the active drug or placebo, plays a critical role in making the hope of finding a cure for ALS a reality.
51 Sites Currently Activated for Regimen E

(as of 10/27/22)

Sites in blue participated in previous regimens. Sites in green (underlined to the side) are new additions to the Platform Trial!

Lehigh Valley Health Network
Mass General Hospital
University of Kansas
University of Maryland
California Pacific Medical Center
Northwestern University
Virginia Commonwealth University
University of Nebraska
Washington University
Wake Forest University
Hospital for Special Care
Saint Alphonsus Regional
University of Massachusetts
Duke University
Barrow Neurological Institute
Georgetown University
Texas Neurology
Beth Israel Deaconess Medical Center
SUNY Upstate
Spectrum Health
Henry Ford Hospital
Essentia Health
University of Southern California
University of South Florida
University of Colorado
Providence Brain and Spine
University of Minnesota
Loma Linda University
University of Iowa
Swedish Medical Center
Ohio State University
University of Cincinnati
Thomas Jefferson University

UC San Francisco
Mayo Rochester
University of Washington
Vanderbilt University
UPMC
Indiana University
Augusta University
University of Utah
Holy Cross Hospital
Penn State Hershey
University of CA, Irvine
Cedars Sinai Medical Center
University of Pennsylvania
Nova Southeastern University
Johns Hopkins University
Columbia University
Stony Brook University
Kaiser, Los Angeles

https://bit.ly/3g2NZr5
Requirements for EAPs

➢ Expanded Access Protocols (EAPs) are FDA regulated

➢ Providing drug via an EAP should not interfere with clinical trials

➢ EAPs are meant for ALS patients who are not eligible for clinical trials
2021-present
- 3 study drugs (Regimens B, C, D)
- 10 sites
- 85 participants
- Funded by philanthropy (study drug donated by manufacturers)
- Safety and clinical data; biomarker data
ACT for ALS

Signed into law on Dec 23, 2021

Section 2: Grants for Research on Therapies for ALS via Intermediate-Size EAPs

Sean M. Healey & AMG Center for ALS awarded NINDS U01 Grant to support Expanded Access for Trehalose (SLS-005)

The Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital has been awarded a grant from the National Institute of Neurological Disorders and Stroke (NINDS) to conduct an intermediate size Expanded Access Protocol (EAP) in Amyotrophic Lateral Sclerosis (ALS). The grant is supported by the ACT for ALS (Accelerating Access to Critical Therapies for ALS Act). This EAP will
Intermediate Size EAP - Trehalose

- In start up now
- Expected to enroll first participants in Q1 2023
- 25 sites
- 70 participants
- NIH-funded (PIs: Babu, Berry, Paganoni)
- Happening in parallel to Regimen E of the HEALEY ALS Platform Trial

Outcomes:
- Long-term safety in a broad population
- Biological impact (as measured by neurofilament light levels)
- Clinical efficacy signal (as compared to natural history cohorts)
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 Cancelations:
November 3rd- Webinar canceled due to annual research conference
November 24th- Webinar canceled for holiday, Happy Thanksgiving!