HEALEY ALS Platform Trial

Weekly Q&A – Oct 13, 2022
The goal of the HEALEY ALS Platform Trial is to screen drugs rapidly and efficiently, get solid answers, and determine next steps.
Shared Infrastructure and Common Protocol Allow for Operational and Scientific Efficiencies

Cuts time in 1/2
Reduces placebo by 1/3
Cuts costs by 1/3

Enroll in HEALEY ALS Platform Trial

Shared infrastructure and common protocol allow sharing of placebo data

Randomization

Participant Flow

Regimen A
Regimen B
Regimen C
Regimen D

Active
Placebo
Active
Placebo
Active
Placebo
Active
Placebo
Shared Placebo
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)
HEALEY ALS Platform Trial

*Initial Regimen Updates – trial gave clear answers and direction, efficient execution (time, resources, less placebo)*

- **February 2022:** Regimen A stopped early for futility

- **September 2022:** Regimen B top line results announced
  * Did not meet the prespecified primary endpoint and there were no statistically significant benefits on key secondary measures; full study results, including data on biomarkers and exploratory measures, are expected in the coming months

- **October 2022:** Regimen C top line results announced
  * While the primary endpoint was not met, a secondary endpoint analysis of survival demonstrated a significant reduction in risk of death or permanently assisted ventilation when adjusting for baseline risk imbalances in the CNM-Au8 regimen for the 30 mg dose; full study results, including data on biomarkers and exploratory measures, are expected in the coming months
Weekly Recordings Available on Website

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.

Visit the Website:
https://bit.ly/3g4kzfv
HEALEY ALS Platform Trial
Ongoing and Upcoming Regimens

Regimens D: ongoing

Regimen E enrolling new participants now

- Regimens F&G in start-up (Calico-AbbVie; Revalesio)

- Three additional Regimens selected for inclusion; working on contracts
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 ALS¹-³

2. Zhang et al, 2014
3. Li et al, 2015
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
BARROW NEUROLOGICAL INSTITUTE

TUESDAY | 4 OCTOBER | 3 PM EDT

Recording Available!


Recording available under “educational webinars” on neals.org
Enrollment Updates (as of Oct 13, 2022)

• 148 individuals have signed informed consent

• 107 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 10/13/22)

Sites in blue participated in previous regimens. Sites in green (underlined to the side) are new additions to the Platform Trial!
Only 10% of people living with ALS participate in clinical trials
 Expanded Access

FDA Definition:

- Sometimes called “compassionate use”
- Potential pathway for a patient with an immediately life-threatening or serious disease or condition
- Allows access to an investigational medical product outside of clinical trials
- Used when no comparable or satisfactory alternative therapy available

https://www.fda.gov/news-events/public-health-focus/expanded-access
Categories of Expanded Access Protocols (EAPs)

- Individual Patient, including emergency use
- Intermediate-size Patient Populations
- Treatment Protocol (large patient population)
Requirements for All EAPs

➢ Patient has a **serious** or **immediately life-threatening** disease or condition; no comparable or satisfactory alternative therapy

➢ **Potential benefit justifies potential risk**; potential risk not unreasonable in context of disease or condition

➢ Providing drug will **not interfere with clinical trials** that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use
EAP Companion To HEALEY ALS PLATFORM TRIAL

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
Community Support to EAPs

EAP COMPANION PROGRAM SUPPORTERS

- Healey Center for ALS
- Clearing Corporation Charitable Foundation
- Eddie and Jo Allison Smith Family Foundation
- Richard Straubitz Foundation
- I AM ALS
- Biohaven
- Clene
- Prilenia
- Elliott & Frantz, Inc.

Community Fundraisers
- Tackle ALS – Team Change ALS
- Ellen Corindia’s Fundraiser
- 2019 Olson Cornhole Tournament
- 2019 Worthington Fore ALS
- 2020 and 2021 Fishing for ALS Warriors
- 2020 and 2021 eALSa For a Cure Pick Your Own Path Walk

- 2020 and 2021 Lori’s Shoes “Hope Is In the Bag”
- 2021 and 2022 MLB Lou Gehrig Day 4-ALS
- 2021 Russ Pallesen Fundraiser for EAP
- 2021 Voices for ALS Golf Tournament
- 2021 The Martha Olson-Fernandez Foundation Golf Tournament
- 2021 Gwendolyn Strong Walk
- TechVs ALS

• Big thanks to countless individual contributors
ACT for ALS

Signed into law on Dec 23, 2021

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

https://bit.ly/3S0a9eb
Clinical trials are essential to develop new treatments for all people living with ALS.

Expanded Access Protocols (EAPs) provide access to new investigational products to people who are not eligible for clinical trials while clinical trials are ongoing.

Data collected in EAPs can help supplement clinical development programs by providing safety, clinical, and biomarker data in broad populations that are typically not evaluated in clinical trials.

The ALS community has created mechanisms to run EAPs in parallel to clinical trials.