HEALEY ALS Platform
Trial Patient Information

An adaptive platform trial designed to accelerate the development of effective and breakthrough treatments for people in ALS.

Video Link:

‘For Patients’ page on MGH website:
The goal of the HEALEY ALS Platform Trial is to screen drugs rapidly and efficiently, get solid answers, and determine next steps.

Screening

Regimen Assignment

(n=160 for each regimen)

Regimen A

Regimen B

Regimen C

Regimen D

Regimen E

3:1 Randomization within each Regimen

Zilucoplan

Verdiperstat

CNM-Au8

Pridopidine

Trehalose

Placebo

Placebo

Placebo

Placebo

Placebo

Shared Placebo

Open Label Extension

Open Label Extension

Open Label Extension

Open Label Extension

Screening

24 weeks on study drug (active:placebo = 3:1)
Recap of Sept. and Oct. Research News

– September 29, 2022: FDA Approval of AMX0035

– September 29, 2022: Verdiperstat/Regimen B Topline Results Released

– September 30, 2022: Grant Funding for Trehalose EAP (Regimen E)
  • https://www.massgeneral.org/neurology/als/news/healeyamg-awarded-ninds-uo1-grant

– October 3, 2022: CNM-Au8/Regimen C Topline Results Released
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

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 Ciene 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.
Regimen E - Trehalose

MECHANISM OF ACTION

**Protein stabilization**

- Normal protein
- Mutant protein
- Mutant proteins form toxic aggregations
- Trehalose inhibits aggregation

**Immediate enhancement of autophagy**

- Untreated cell
- Phagophore forming around abnormal proteins
- Autophagosome
- Degrades proteins
- Cell treated with trehalose
- Glucose transporter
- Degrades more proteins

**Prolonged enhancement of lysosomal pathways thus autophagy**

- Cell treated with trehalose
- TFEB activates CLEAR (lysosomal and autophagy) genes
- Enhanced expression of lysosomal proteins
- Building more lysosomes
- Degrades oligo fats and sugars

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   Available at: https://www.nature.com/articles/srep38586#f1 Accessed February 2019.

Informational Webinars about Regimen E

Trehalose/SLS-005 Drug Science and Mechanism of Action Q&A Webinar
Hosted by Seelos Therapeutics on 10 March 2022

Recording Available!

Recording available under “science and mechanism of action series”

The ALS Association/Northeast ALS Consortium Educational Webinar

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

Recording Available!

Recording available under “educational webinars” on neals.org
57 Sites Currently Activated for Regimen E

(as of 11/10/22)

Sites in blue participated in previous regimens. Sites in green (underlined to the side) are new additions to the Platform Trial!
Enrollment Updates (as of Nov 10, 2022)

• 164 individuals have signed informed consent

• 121 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
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 Cancellation:
November 24th - Webinar canceled for holiday, Happy Thanksgiving!