The HEALEY ALS Platform Trial is a Perpetual Adaptive Trial

3:1 Randomization within each Regimen

Regimen A
- Zilucoplan
- Placebo

Regimen B
- Verdiperstat
- Placebo

Regimen C
- CNM-Au8
- Placebo

Regimen D
- Pridopidine
- Placebo

Regimen E
- Trehalose
- Placebo

Shared Placebo

(n=120 for active drug; n=40 for placebo)

(n=160 for each regimen)
Enrollment Updates (as of July 28, 2022)

- 96 individuals have signed informed consent
- 66 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.
41 Sites Currently Activated for Regimen E

(as of 7/28/22)

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

https://bit.ly/3g2NZr5

Site Map & Contacts:
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 Guest Speakers:
August 4th - Cancelled
August 11th - TBD
August 18th - Amanda Peltier, MD, MS (Site Investigator at Vanderbilt University in TN)
Guest Speaker

Lori Chibnik, PhD, MPH
Assistant Professor & Biostatistician
Harvard TH Chan School of Public Health & MGH
Trial Statisticians

MGH Biostatistics

Eric Macklin, PhD; Lori B. Chibnik, PhD, MPH; Douglas Hayden, PhD; Marie-Abele Bind, PhD; PoYing Lai, MS

Berry Consultants

Michelle Detry, PhD; Melanie Quintana, PhD; Ben Saville, PhD; Matteo Vestrucci, PhD
PLACEBOS
• What is a placebo
• Why do we need them?
• What is a placebo effect (in ALS)?
• Can we use placebos from previous trials?
What is a placebo?

• A “sugar pill”?

• Something that is identical to the active drug, but without the active ingredient.
  – Identical in look, weight, taste, smell, dose, all properties
  – Only way to tell it is placebo is by chemical analysis
The goal of a clinical trial is to show that a drug is safe and effective. We need to show that any efficacy and adverse events are the result of the drug and only the drug. The design of a double-blind clinical trial – where neither participant, nor researcher knows which drug someone is getting – is the best way to determine this.
What is the Placebo Effect – in general

• a beneficial health outcome resulting from a person's anticipation that an intervention will help
• Placebo effect is seen more in *subjective* measures than *objective* measures
• Some interesting examples
  – *higher* dose placebos are more effective than *lower* dose placebos
  – *more* expensive placebos are more effective than *less* expensive placebos
Placebo Effect in ALS

• ALS progression has very little subjectivity, however the placebo effect can also be seen in objective measures

• Examples:
  – An open-label trial of lithium in a small number of patients suggested this drug helped slow the disease. But a larger, placebo-controlled, double-blind trial found no effect
  – Animal studies and open-label human trials suggested the antibiotic minocycline was beneficial. But a larger, placebo-controlled trial showed it was not, and may even have been harmful.
Can we use placebos from previous trials?

- Remember: We need to show that any efficacy and adverse events are the result of the drug and only the drug.
- Any differences between previous study and current study mean we cannot know if it is the drug that is the reason for the differences.
- Examples:
  - Differential selection of patients, different consent criteria
  - Changes in standard of care (e.g. edaravone)
  - Different studies have different data quality and completion
Questions?

I became a comedian because I feel that laughter is the best medicine.

I've seen your act. It's a placebo.
HEALEY ALS Platform trial

**Study design**
- ‘clinically meaningful’ results
- Sample Size
- Randomization

**Consent to Platform**
- Regimen A
  - Drug A (n=120)
  - Placebo A (n=40)
- Regimen B
  - Drug B (n=120)
  - Placebo B (n=40)
- Regimen C
  - Drug C1 (n=60)
  - Drug C2 (n=60)
  - Placebo C (n=40)
- Regimen D
  - Drug D (n=120)
  - Placebo D (n=40)
- Regimen E
  - Placebo ABCD (n~120)

**Analysis**
- Drug A (n ≤ 160)
- Drug B (n ≤ 160)
- Drug C1 (n ≤ 80)
- Drug C2 (n ≤ 80)
- Drug D (n=120)