The HEALEY ALS Platform Trial is a Perpetual Adaptive Trial

**Regimen A** (n=160 for each regimen)
- Zilucoplan
  - Placebo
- Verdiperstat
  - Placebo
- CNM-Au8
  - Placebo
- Pridopidine
  - Placebo

**Regimen B**
- Open Label Extension

**Regimen C**
- Open Label Extension

**Regimen D**
- Open Label Extension

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

Shared Placebo
Regimens A, B and C completed enrollment!

- 162 individuals were randomized within Regimen A
- 167 individuals were randomized within Regimen B
- 161 individuals were randomized within Regimen C
- 159 individuals were randomized within Regimen D

324 have entered the Open Label Extension (OLE)

>800 people with ALS signed Informed Consent for the Platform Trial

“I’m looking forward to helping find a cure for ALS.”
- Platform trial participant

Thank You

This breakthrough trial would not be possible without your partnership

as of 12/16/21
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**Screening**
(n=160 for each regimen)

**Regimen Assignment**

- **Regimen A**
- **Regimen B**
- **Regimen C**
- **Regimen D**
- **Regimen E**

3:1 Randomization within each Regimen

- **Zilucoplan**
  - Placebo
- **Verdiperstat**
  - Placebo
- **CNM-Au8**
  - Placebo
- **Pridopidine**
  - Placebo
- **Trehalose**
  - Placebo

Shared Placebo

Open Label Extension
Send us webinar ideas!

Upcoming Guest Speakers:
Dec 23\textsuperscript{rd} - No Webinar
Dec 30\textsuperscript{th} - No Webinar
Jan 6\textsuperscript{th} - Guest TBD
Jan 13\textsuperscript{th} - Sharon Hesterlee, PhD of the Muscular Dystrophy Association
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; James Chan, MA; PoYing Lai, MS

Berry Consultants

Michelle Detry, PhD; Melanie Quintana, PhD; Ben Saville, PhD; Matteo Vestruci, PhD
• Curated questions from
  – Past webinars
  – Facebook sessions and AMA
  – Emailed questions

What determined n=160 as the magic number for each regimen?

How does the platform randomization work given that there are 3 drugs that have over 200 patients enrolled, the placebo, and now Pridopidine is new with just 1 patient?

For the next round, will the current placebo data be combined with that to be acquired in the next round?

One of the slides mentioned a non-statistically significant difference. Can you explain that please, since you were so positive on the positive results.

How are deaths included in the statistical analysis of adverse consequences if the death is from ALS and not trial complications?

How come trials are set up in a way to “prove statistical significance”, but even when they are deemed “positive”, they are not “significant” ENOUGH for the FDA?

If someone re-randomizes into a second regimen, is it possible then could be randomized into placebo 2x?

Can you explain to people how the FDA's statistical penalty works for manufacturers who decide to do an interim analysis and how you or a manufacturer decides if they will be doing those in the Healey trials?
ALS PLATFORM TRIAL THROUGH THE EYES OF A STATISTICIAN
Healey ALS Platform trial

Study design
‘clinically meaningful’ results
Sample Size
Randomization

Consent to Platform

Regimen A
Drug A (n=120)
PlaceboA (n=40)

Regimen B
Drug B (n=120)
PlaceboB (n=40)

Regimen C
Drug C1 (n=60)
Drug C2 (n=60)
PlaceboC (n=40)

Regimen D
Drug D (n=120)
PlaceboD (n=40)

Regimen X
PlaceboABCD (n~120)

Analysis

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

Sample Size

Randomization

Study design
‘clinically meaningful’ results

Consent to Platform

Regimen A
Drug A (n=120)
PlaceboA (n=40)

Regimen B
Drug B (n=120)
PlaceboB (n=40)

Regimen C
Drug C1 (n=60)
Drug C2 (n=60)
PlaceboC (n=40)

Regimen D
Drug D (n=120)
PlaceboD (n=40)

Regimen X
PlaceboABCD (n~120)

Analysis

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