• To submit text questions to today’s presenters, please type your questions into the ‘Q&A’ box

• Today’s presentation is being recorded and will be posted on the Healey & AMG Center for ALS website

https://www.massgeneral.org/neurology/als/research/platform-trial
HEALEY ALS Platform Trial

Updates – Nov 30, 2020

Merit Cudkowicz
Healey & AMG Center

Sabrina Paganoni
Healey & AMG Center

Jennifer DiMartino
ALS ONE
BRINGING TOGETHER A COMMUNITY
to launch the first platform trial for ALS
ALS ONE provides care today, while uniting research for a cure tomorrow.

Research
A partnership of world-leading ALS researchers focused on a cure

Care
Providing care and essential resources for those who need it most

Fundraising
Critical funding is necessary to further our united research and care
AGENDA

• Updates on the HEALEY ALS Platform Trial
  - Study Treatments
  - Sites
  - Enrollment
  - COVID impact

• How to stay in touch and find a site near you

YOUR QUESTIONS
# Accelerating ALS Therapy Development

## Traditional

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Disease</th>
<th>Treatment A</th>
</tr>
</thead>
</table>

## Platform

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Disease</th>
<th>Treatment A</th>
<th>Treatment B</th>
<th>Treatment C</th>
<th>Treatment D</th>
</tr>
</thead>
</table>
Perpetual Adaptive Trial
Randomization Ratio 3:1; Shared Placebo
Open Label Extension offered

Screening
Regimen Assignment
(n=160 for each regimen)

Regimen A
Regimen B
Regimen C
Regimen D

3:1 Randomization within each Regimen

Zilucoplan
Placebo

Verdiperstat
Placebo

CNM-Au8
Placebo

Pridopidine
Placebo

Shared Placebo

Screening
24 weeks on study drug (active:placebo = 3:1)
We want to keep adding great therapies

- Submissions accepted on a rolling basis
- We opened with 3 regimens (zilucoplan, verdiperstat, CNM-Au8)
- The 4th regimen is being added (pridopidine)
- We are in discussions with 3 additional companies for 2021!

https://www.massgeneral.org/neurology/als/research/platform-trial
Platform Trial – Target Population

Key Inclusion Criteria

• Sporadic or familial ALS (possible, probable, lab-supported probable, or definite by revised EEC)
• Time since onset of weakness due to ALS ≤ 3 years (36 months)
• Slow vital capacity (SVC) ≥ 50% of predicted capacity for age, height, and sex
• Able to swallow
• Participants must either not take riluzole or be on a stable dose of riluzole for ≥ 30 days
• Participants must either not take edaravone or have completed at least one cycle of edaravone

Sample Size: 160 per regimen (120 on active and 40 on placebo)

Treatment Duration: 24 weeks + Open Label Extension
Platform Trial – Endpoints

Primary Endpoint
Change in disease severity - ALS Functional Rating Scale-Revised (ALSFRS-R) + Mortality

Secondary Endpoints
1. Change in respiratory function - slow vital capacity (SVC)
2. Change in muscle strength - hand held dynamometry (HHD)
3. Survival
4. Treatment-specific biomarkers as applicable

Safety Endpoints

Exploratory Endpoints
Exploratory Endpoints

DNA
Neurofilaments
Biomarkers (Blood, Urine, CSF)
Speech Analysis
Home Spirometry

Endpoint Development Engine
List of enrolling sites as of Nov 30, 2020
31 sites are enrolling

- Texas Neurology
- MGH
- UTHSCSA
- Hospital for Special Care
- Holy Cross Hospital
- Thomas Jefferson
- Houston Methodist
- Henry Ford Health System
- Barrow Neurological Institute
- Ohio State University
- Northwestern University
- University of Chicago
- Wake Forest
- University of Nebraska Medical Center
- Loma Linda
- University of Washington
- University of Iowa
- Washington University
- University of Pennsylvania
- University of Michigan
- Forbes Norris MDA/ALS Research Center, CPMC
- Penn State Hershey
- UMass
- University of Miami
- University of Colorado
- Cedars-Sinai
- University of Florida
- University of South Florida
- Columbia University
- University of Virginia
- Emory
How to Find a Center Near You

* 31 sites are actively enrolling

Contact Info of Participating Sites by State

https://www.massgeneral.org/neurology/als/research/platform-trial-sites
Patient Navigator

Catherine Small
Allison Bulat

Phone: 833-425-8257 (HALT ALS)
E-mail: healeyalsplatform@mgh.harvard.edu
How to Receive Platform Trial Updates

Sign up for the ALS Link Newsletter (for info on this trial and other research opportunities)

https://www.massgeneral.org/neurology/als/services/clinical-trials-enrollment-coordination
Enrollment Updates (as of Nov 30, 2020)

- 209 individuals with ALS signed informed consent
- 162 individuals were assigned to a regimen
- 131 are currently receiving study drug (active or placebo)

*We will continue to update the ALS community on enrollment (website, webinars)*
INITIAL COVID-19 IMPACT

- Most centers experienced major disruptions to normal workflow
- Limited to no ability to start new studies / enroll new research participants (prohibited at many sites)
- Staff redeployment and furloughs
- Substantial restrictions on staff access to the clinic and research areas with most staff working remotely
- Restrictions on certain procedures (respiratory function tests)
- Regional variability means that some sites have experienced different barriers at different times which affected their timelines
We remained committed to the trial through COVID and were able to start the trial despite the pandemic

• Lots of activities happened remotely in the spring
  - Training, contracts, and administrative tasks to enable site activation

• Protocol amendments made the trial “COVID resilient”
  - Home spirometry
  - Telemedicine for some visits
  - Home labs for some visits

Enrollment Started in July 2020 and has been exceeding expectations at sites that were able to open
CURRENT COVID-19 IMPACT

• Many centers are experiencing a second surge
  - staff redeployment
  - some institutions are limiting research activities

• Supply chain problems (central vendor)
• Cyberattacks
• Home nursing shortages
For More Updates

• **Weekly webinars**
  The idea of came from our Patient Advisory Committee: we are excited to be talking with you on a weekly basis and take any questions you might have

• **Find the schedule and registration links on our website**
  https://www.massgeneral.org/neurology/als/research/platform-trial-news/

**Coming up: webinars about each drug’s mechanism of action and science**