Thank you for joining the weekly webinar!
We are admitting audience members from the waiting room.

Please allow a few moments for the webinar to begin.
Hilda Gutierrez, MD
Research Operations Coordinator
Beth Israel Deaconess Medical Center
Boston, MA
HEALEY ALS Research Team at BIDMC

Dr. Courtney McIlduff
Principal Investigator

Dr. Seward Rutkove
Sub-Investigator

Hilda Gutierrez
Lead Study Coordinator

Soleil Samaan
Study Coordinator

Diane Healy
Study Nurse
HEALEY ALS Platform Trial:

Common Protocol and Shared Infrastructure

- Regimen A
- Regimen B
- Regimen C
- Regimen D
- Regimen E
- Regimen F
- Regimen G

Screen for eligibility → Randomization 3:1 → Active

ENROLLMENT COMPLETE

Screening Period
Randomized Period (24 weeks)
Open-Label Extension Period (Active Treatment Extension)

ENROLLING

SEELOS THERAPEUTICS

Calico

JENALI THERAPEUTICS
Adaptive Platform Trials to Transform Amyotrophic Lateral Sclerosis Therapy Development

Sabrina Paganoni, MD, PhD,1,2# James D. Berry, MD, MPH,1# Melanie Quintana, PhD,3#
Eric Macklin, PhD,4 Benjamin R. Saville, PhD,3,5 Michelle A. Detry, PhD,3
Marianne Chase, BA,1 Alexander V. Sherman, MSc,1 Hong Yu, MS,1 Kristin Drake, MBA,1
Jinsy Andrews, MD,6 Jeremy Shefner, MD, PhD,7 Lori B. Chibnik, PhD, MPH,4
Matteo Vestrucci, PhD,3 Merit E. Cudkowicz, MD, MSc,1

and for the Healey ALS Platform Trial Study Group

Current therapeutic development in amyotrophic lateral sclerosis (ALS) relies on individual randomized clinical trials to test a specific investigational product in a single patient population. This approach has intrinsic limitations, including cost, time, and lack of flexibility. Adaptive platform trials represent a novel approach to investigate several interventions for a single disease in a continuous manner. Already in use in oncology, this approach is now being employed more often in neurology. Here, we describe a newly launched platform trial for ALS. The Healey ALS Platform Trial is testing multiple investigational products concurrently in people with ALS, with the goal of rapidly identifying novel treatments, biomarkers, and trial endpoints.

ANN NEUROL 2022;00:1–11

Design and Statistical Innovations in a Platform Trial for Amyotrophic Lateral Sclerosis

Melanie Quintana, PhD,1 Benjamin R. Saville, PhD,1,2 Matteo Vestrucci, PhD,1
Michelle A. Detry, PhD,1 Lori Chibnik, PhD, MPH,3,4 Jeremy Shefner, MD, PhD,5
James D. Berry, MD, MPH,6,7 Marianne Chase, BA,6,7 Jinsi Andrews, MD,8
Alexander V. Sherman, MSc,6,7 Hong Yu, MS,6,7 Kristin Drake, MBA,6,7
Merit Cudkowicz, MD, MSc ©,6,7 Sabrina Paganoni, MD, PhD,6,7,9 Eric A. Macklin, PhD,4,5
for the HEALEY ALS Platform Trial Study Group

Platform trials allow efficient evaluation of multiple interventions for a specific disease. The HEALEY ALS Platform Trial is testing multiple investigational products in parallel and sequentially in persons with amyotrophic lateral sclerosis (ALS) with the goal of rapidly identifying novel treatments to slow disease progression. Platform trials have considerable operational and statistical efficiencies compared with typical randomized controlled trials due to their use of shared infrastructure and shared control data. We describe the statistical approaches required to achieve the objectives of a platform trial in the context of ALS. This includes following regulatory guidance for the disease area of interest and accounting for potential differences in outcomes of participants within the shared control (potentially due to differences in time of randomization, mode of administration, and eligibility criteria). Within the HEALEY ALS Platform Trial, the complex statistical objectives are met using a Bayesian shared parameter analysis of function and survival. This analysis serves to provide a common integrated estimate of treatment benefit, overall slowing in disease progression, as measured by function and survival while accounting for potential differences in the shared control group using Bayesian hierarchical modeling. Clinical trial simulation is used to provide a better understanding of this novel analysis method and complex design.

ANN NEUROL 2023;00:1–14

Design and Statistical Innovations in a Platform Trial for Amyotrophic Lateral Sclerosis - Quintana - Annals of Neurology - Wiley Online Library
Enrollment Update: Regimen F (as of 6/29/23)

150
Participants consented to Master Protocol since RGF initiated

99
Participants assigned to RGF

76
Participants randomized within RGF (enrollment goal ≈240)

Thank You
for your partnership in ALS research
58 Sites Currently Active for Regimen F

(as of 6/29/23)

Nova Southeastern University
Essentia Health
Texas Neurology
Mass General Hospital
University of Nebraska
Hospital for Special Care
Henry Ford Hospital
Augusta University
Beth Israel Deaconess
University of Texas HSC
University of Colorado
Loma Linda University
Ohio State University
Cedars Sinai Medical Center
Duke University
Wake Forest University
Saint Alphonsus
UMass Worcester
Lehigh Valley
Thomas Jefferson
University of South Florida
University of Pennsylvania
SUNY Upstate
University of Iowa
California Pacific Med Center
Houston Methodist
Vanderbilt University
University of Minnesota
Washington University
Barrow Neurological Institute
University of Miami
Temple University
University of Virginia
Johns Hopkins University
University of Southern CA
Holy Cross Hospital

University of Washington
University of Utah
Penn State Hershey
University of Michigan
University of Kansas
Stony Brook University
University of Cincinnati
Mayo Clinic Rochester
Northwestern University
Georgetown University
Kaiser, Los Angeles
University of Pittsburgh
Virginia Commonwealth
Med College Wisconsin
University of CA, San Fran
University of Florida, Gainesville
Providence Brain and Spine
Cleveland Clinic
George Washington University
Hackensack University
Swedish Medical Center
University of Kentucky

https://bit.ly/3g2NZr5
Enrollment Update: Regimen G (as of 6/29/23)

102
Participants consented to Master Protocol since RGG initiated

20
Participants assigned to RGG

14
Participants randomized within RGG (enrollment goal ≈240)

Thank You
for your partnership in ALS research
18 Sites Currently Active for Regimen G

(as of 6/29/23)

Nova Southeastern University
Texas Neurology
University of Colorado
Essentia Health
University of Pittsburgh
Beth Israel Deaconess
Mass General Hospital
Ohio State University
University of Michigan
Hospital for Special Care
Vanderbilt University
Henry Ford
University of Iowa
University of Nebraska
Lehigh Valley
CMC
University of Pennsylvania
SUNY Upstate

https://bit.ly/3g2NZr5
Checking Site Status Online

List of Participating Sites

Sites marked "Recruiting" are currently enrolling participants. Sites marked "Active, Not recruiting" are active in the Platform Trial (for example, they are following participants in ongoing regimens that have already completed enrollment) but are not enrolling new participants at this time.

<table>
<thead>
<tr>
<th>Site</th>
<th>State</th>
<th>Enrollment Status</th>
<th>Trial Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrow Neurological Institute</td>
<td>AZ</td>
<td>Recruiting</td>
<td>Whitney Dailey</td>
</tr>
<tr>
<td>Cedars-Sinai Medical Center</td>
<td>CA</td>
<td>Recruiting</td>
<td>Sophia Mostowy</td>
</tr>
<tr>
<td>Forbes Norris MDA/ALS Research Center, California Pacific Medical Center</td>
<td>CA</td>
<td>Recruiting</td>
<td>Teji Dulai</td>
</tr>
<tr>
<td>Kaiser Permanente, Los Angeles Medical Center</td>
<td>CA</td>
<td>Recruiting</td>
<td>Mary H. Berganza</td>
</tr>
</tbody>
</table>

Contact a study team near you to discuss enrollment opportunities.

https://bit.ly/3g2NZr5
Regimen G Drug Science Q&A Webinar

Topic: DNL343 Drug Science and Mechanism of Action

Link to Register: https://bit.ly/3NqJU1j

Open to everyone!
Thursday, July 20th
5:00-6:00pm Eastern
EDUCATIONAL WEBINAR
UNDERSTANDING STATISTICAL AND CLINICAL SIGNIFICANCE

SPEAKERS
JINSY ANDREWS, MD, MSc
COLUMBIA UNIVERSITY

CHRISTINA FOURNIER, MD, MSc
EMORY UNIVERSITY

ERIC MACKLIN, PhD
HARVARD MEDICAL SCHOOL

What do researchers and scientists mean when they describe a study as “statistically significant?” How do people with ALS and clinicians understand whether or not a treatment option is “clinically significant?” This webinar and panel discussion will provide a framework for understanding the results of ALS clinical trials, using several recent studies as examples.

View Here:
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 Webinars:
July 6th - Weekly Q&A with Bill Cho MD, PhD from Calico Life Sciences (Regimen F)
July 13th - Weekly Q&A with Sarah Heintzman, APRN-CNP (Ohio State University)
July 20th - Regimen G / DNL343 Drug Science Q&A Webinar with Denali