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.
HEALEY ALS Platform Trial

Weekly Q&A – June 22, 2023
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
Placebo
Active

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

ENROLLMENT COMPLETE
ENROLLING
ENROLLING
## 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](https://bit.ly/3g2NZr5)
Enrollment Update: Regimen F (as of 6/22/23)

Participants consented to Master Protocol since RGF initiated

Participants assigned to RGF

Participants randomized within RGF (enrollment goal ≈240)

Thank You
for your partnership in ALS research
Enrollment Update: Regimen G (as of 6/22/23)

- **84** Participants consented to Master Protocol since RGG initiated
- **17** Participants assigned to RGG
- **7** Participants randomized within RGG (enrollment goal ≈240)

Thank You for your partnership in ALS research
Visit Our Website

Reg F and Reg G Resources on MGH Website

Reg F and Reg G Resources on MGH Website

Visit Our Website

Printable Brochures Available!

HEALEY ALS Platform Trial

Regimen F

ABV-CL-7572

Developed by Genzyme and Genzyme Ireland in collaboration with ABVx Inc.

Regimen F is a Phase 2/3 trial enrolling approximately 240 participants to evaluate the safety and efficacy of ABV-CL-7572 as a potential treatment for ALS. This regimen involves biomarker analysis and exploratory clinical outcomes via further procedures to assess the success of ABV-CL-752.

Q&A about Regimen F:

1. How is this drug administered? A. ABV-CL-7572 is taken by mouth once daily. The study drug is mixed with small packets of water and has a granular texture similar to sugar, so should be swallowed with a mouthful of water.

2. What dose is this drug? A. ABV-CL-7572 aims to reduce function in cells of motor neurons by normalizing protein production and producing further buildup of TDP-43, thereby promoting errors, and possibly slowing ALS progression. ABV-CL-7572 activates the protein complex eIF2, which is a key regulator of the integrated stress response (ISR). Studies suggest that the ISR is chronically activated in people with ALS, and that TDP-43 aggregates, a hallmark of ALS, may have a role in chronic ISR activation. Binding of ABV-CL-7572 decreases eIF2ß stress to stress and decreases the ISR, which may prevent motor neuron injury in ALS.

3. Has this drug been studied before? Yes. A Phase I/II human study of ABV-CL-7572 showed that the drug was well tolerated by participants, and crossed the dose barrier to demonstrate safety and clinical efficacy.

4. What are the potential side effects of this drug? A. Most participants who received ABV-CL-7572 in the Phase I/II study experienced mild or moderate adverse effects. These included flu-like symptoms, fatigue, nausea, and vomiting.

5. Is this drug FDA approved? A. No, ABV-CL-7572 has not been approved by the FDA.

About Regimen G:

Regimen G is a Phase 2/3 trial enrolling approximately 240 participants to evaluate the safety and efficacy of DNL-534 as a potential treatment for ALS. This regimen involves biomarker analysis and exploratory clinical outcomes via further procedures to assess the success of DNL-534.

Q&A about Regimen G:

1. How is this drug administered? A. DNL-534 is taken by mouth once daily. The study drug is in the form of capsules that are stored in small packets (sachets) and has a granular texture similar to sugar, so should be swallowed with a mouthful of water.

2. What dose is this drug? A. DNL-534 is designed to inhibit the ISR, reduce protein aggregation, and increase TDP-43-containing neuronal protein, which may improve cellular function in ALS.

3. Has this drug been studied before? A. Yes. Prior studies showed that DNL-534 is generally well tolerated in individuals living with ALS and healthy participants. DNL-534 administration led to a reduction in two ISR biomarkers in the blood, suggesting that DNL-534 inhibits the ISR. Analysis of participants CPE (the ratio that increases when cells are exposed to stress) showed that DNL-534 was well tolerated in individuals living with ALS and healthy participants.

4. What are the potential side effects of this drug? A. Most participants who received DNL-534 in the Phase I/II study experienced mild or moderate adverse effects. These included flu-like symptoms, fatigue, nausea, and vomiting.

5. Is this drug FDA approved? A. No, DNL-534 has not been approved by the FDA.

About NEALS:

Visit Our Website

Visit our website to learn more about new and future regimens; more investigational products are anticipated to be added to the HEALEY ALS Platform Trial through support by pharma, foundation partners, philanthropists, federal, and other funding initiatives.

Visit this website for more information on the HEALEY ALS Platform Trial:

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
Guest Speaker

Shafeeq Ladha, MD
Platform Trial Site Investigator
Barrow Neurological Institute (Phoenix, AZ)
Link to Lumbar Puncture Short Video:
https://www.youtube.com/watch?v=3omIOEnll8o
Regimen F: ABBV-CLS-7262, by Calico and AbbVie - Now Recruiting

ABBV-CLS-7262 is an investigational drug developed by Calico Life Sciences LLC in collaboration with AbbVie Inc. ABBV-CLS-7262 aims to restore function in cells affected by ALS by normalizing protein synthesis and preventing further sequestration and aggregation of TDP-43, thereby protecting neurons, and possibly slowing ALS progression.

This integrated stress response (ISR) is a fundamental transduction process that regulates cell function during various stressful conditions. Tissue studies suggest that the ISR is chronically induced in people with ALS. It is proposed that TDP-43 aggregates, a hallmark feature in the motor neurons of people with ALS, could be formed by a chronically induced ISR. ABBV-CLS-7262 activates the protein complex eIF2B, which is a key regulator of the ISR. Binding of ABBV-CLS-7262 desensitizes eIF2B to stress and decreases the ISR. Reduction of the ISR restores normal protein synthesis, reduces TDP-43 sequestration in stress granules, and may decrease TDP-43 aggregation.

A prior first-in-human study of ABBV-CLS-7262 showed that this drug was well-tolerated by participants, demonstrated target engagement by increasing eIF2B enzymatic activity, and suppressed the ISR in blood cells. ABBV-CLS-7262 crossed the blood brain barrier at concentrations predicted to be efficacious in ALS. ABBV-CLS-7262 is currently being investigated in a Phase 1b study in people with ALS (NCT04948845), and will be studied further as part of the HEALEY ALS Platform Trial.

Watch a webinar about the science behind ABBV-CLS-7262

Watch this video for more information on the mechanism of action behind ABBV-CLS-7262.

Download Regimen F Brochure
Download Lumbar Puncture Brochure

Understanding HEALEY ALS Platform Trial Study Procedures

Lumbar Puncture

A Lumbar Puncture (LP), or Spinal Tap, is a procedure to remove a small sample (10-30ml, or -6 tablespoons) of cerebrospinal fluid (CSF) from the lower spine. CSF is the fluid that surrounds the brain and spinal cord. It contains proteins, cells, and other substances that are important markers in ALS research. During the procedure, a needle is inserted between two lumbar vertebrae (lumbaros) in the lower back and into the space in the spinal cord that contains CSF.

If you experience pain during the needle insertion, there may be a chance of experiencing side effects. The needle is inserted into the space in the spinal cord, so do not push too deep into the tissues or flex your spine.

Tips to Prep:

Get a good night's rest, eat as usual, and stay well-hydrated prior to the LP visit.

At your visit, the doctor will ask you to sit or lie down in a position that helps widen the spaces between the bones of the lumbar spine.

1. The doctor will clean the skin on your lower back to reduce the risk of infection, then use a small needle to inject a local anesthetic (such as lidocaine) to numb the site.
2. The nurse will place sterile drapes around the injection site.
3. The nurse will insert the needle into the spinal fluid (CSF) and collect CSF.
4. The nurse will remove the needle and apply a band-aid to the site.
5. You should feel nothing after the procedure.
6. If you experience pain, you should report it to the doctor immediately.

Printable Lumbar Puncture Info Sheet!

For more information about the study, visit https://bit.ly/3SIwH4X