Adaptive platform trial hopes to bring new treatments to patients faster

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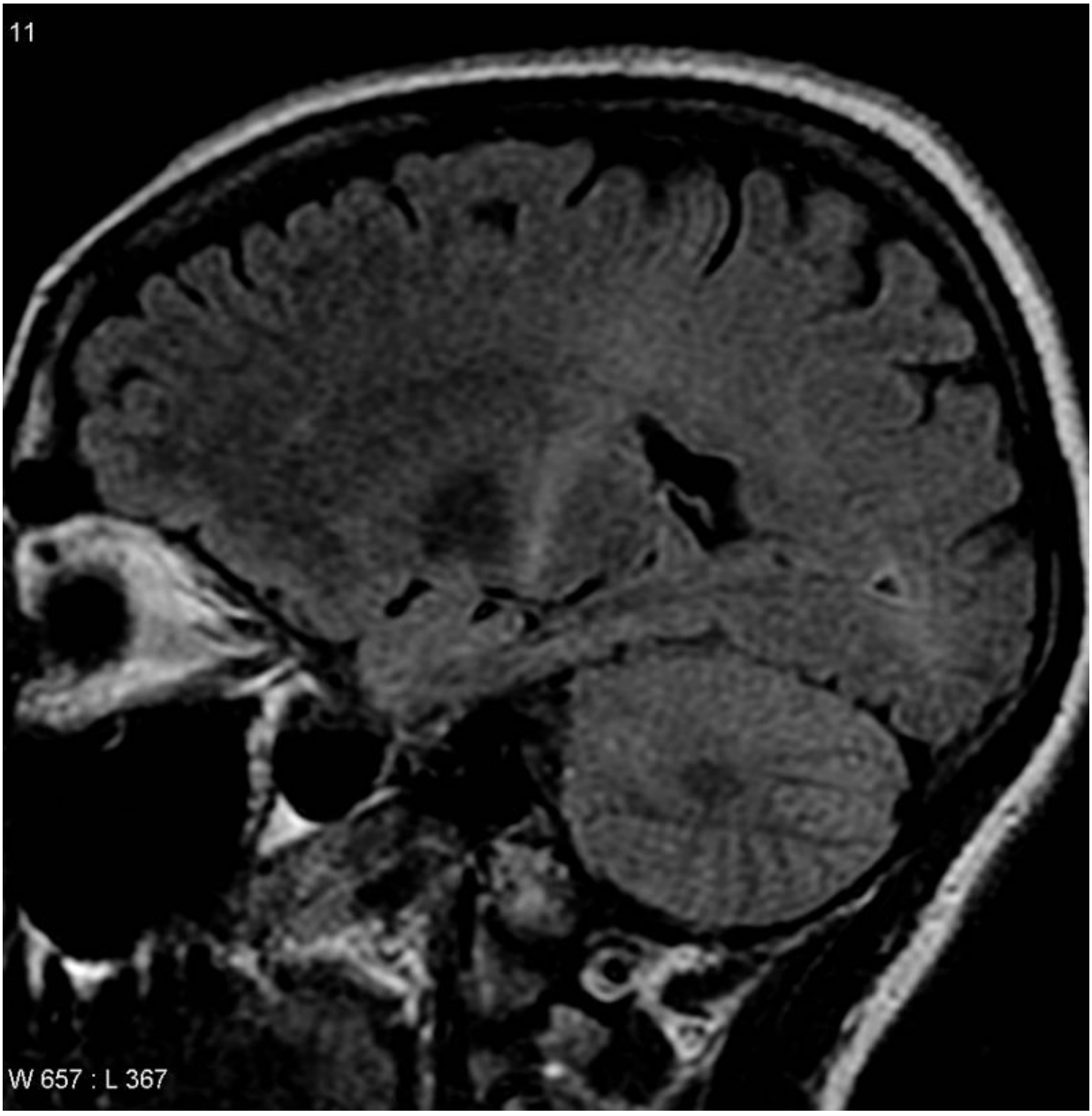

An MRI with increased signal in the posterior part of the internal capsule which can be tracked to the motor cortex consistent with the diagnosis of ALS. Credit: Frank Gaillard/Wikipedia

A new paper in *Annals of Neurology* describes the approach, structure, and launch of the HEALEY ALS Platform Trial—the first platform trial for amyotrophic lateral sclerosis (ALS)—designed to accelerate the development of effective and breakthrough treatments for people with the illness.

"This study is really the first comprehensive platform for ALS drug development, where a central infrastructure is shared between a variety of investigational products, each tested using a common protocol and compared to a shared placebo cohort," says first author and co-principal investigator Sabrina Paganoni, MD, Ph.D., co-director of the Massachusetts General Hospital (MGH) Neurological Clinical Research Institute (NCRI), physician scientist at the Healey & AMG Center for ALS at Mass General, and assistant professor of PM&R at Harvard Medical School and Spaulding Rehabilitation Hospital. "Due to this design, people living with ALS who participate in this trial have a greater chance of receiving an active treatment."

Under the leadership of Paganoni and principal investigator Merit Cudkowicz, MD, MSc, director of the Sean M. Healey and AMG Center for ALS, chief of Neurology at MGH and the Julieanne Dorn Professor of Neurology at Harvard Medical School, the HEALEY ALS Platform Trial enrolls patients across a network of more than 50 coordinated sites of the NEALS Consortium nationwide. The trial simultaneously evaluates several treatments on an ongoing basis.

"The trial has several important scientific goals as we are collecting a number of novel biomarkers and outcome measures which could provide more efficient readouts not only for this trial for the entire ALS clinical trial landscape," says Cudkowicz. "Further, we are creating an approach that ensures data sharing and sample sharing from the growing placebo cohort where we hope we can contribute to our understanding of the science behind ALS and share the learnings in a collaborative manner."

Currently, the HEALEY ALS Platform Trial has completed enrollment in its first four trial arms and testing of a fifth investigational product has already begun. "An important feature of the trial is that it will be evergreen, meaning that we intend to always have multiple investigational products available to new participants," says Paganoni. The team is working with more industry collaborators to create new treatment spots in 2022 with a plan for many more after that.

Since its inception in summer 2020, more than 800 patients have enrolled in the HEALEY ALS Platform trial, with about 160 participants assigned to the first four trial arms. Results from these first four studies are expected later in 2022. "Because of the platform nature of the study and the use of a shared placebo group, the active to placebo ratio is very favorable for participants, three to one in favor of receiving an active drug," says Paganoni. "That is simply not possible with traditional standalone trials," she says. The trial design allows all participants to receive active treatment as part of a long-term Open Label Extension (OLE) after six months of randomized, placebo-controlled trial participation. In addition to granting access to active drug, the OLE will provide important scientific data about the long-term safety and efficacy of the investigational products tested in the trial.

The HEALEY ALS Platform Trial has invigorated the ALS clinical trials landscape, and there has been resounding support from the patient community. Enrollment has been exceeding expectations, which is

remarkable considering that the trial's launch coincided with the COVID-19 pandemic.

"We are grateful to the members of our patient advisory committee, who have been working with us to design a patient-centric trial with more access opportunities," says Paganoni. "This trial would not be possible without the generous contributions of hundreds of people with ALS and their families and supporters who decided to devote their time and efforts to ALS research to benefit the entire ALS scientific and patient family during these challenging pandemic times."

More information: Sabrina Paganoni et al, Adaptive Platform Trials to Transform Amyotrophic Lateral Sclerosis Therapy Development, *Annals of Neurology* (2021). DOI: 10.1002/ana.26285

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