PROVIDENCE
Brain and
Spine Institute

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PROVIDENCE ALS CENTER

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ALS Newsletter – Research Special Edition

Since Providence ALS Center opened, we have actively engaged in research to advance knowledge of and treatments for the disease. As Oregon's largest Center of Excellence for ALS, we offer comprehensive care. Participating in clinical trials that offer our patients access to cutting-edge therapies is an essential part of our holistic approach.

Even amidst COVID, our research efforts remain strong. We are thrilled to be recruiting for several active studies right now and are dedicating this issue of our newsletter to this topic. The following pages are details on each study, including the groundbreaking HEALEY ALS Platform Trial. Providence ALS Center is one of just 52 sites in the nation, and the only site in Oregon, conducting this trial, which offers a new way to test multiple experimental treatments at once to reduce research costs, increase patient participation, and accelerate the pace of research.

If you are interested in learning more about any of these opportunities, please visit our website or contact our clinic.

https://oregon.providence.org/our-services/c/clinical-trials-brain

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Providence ALS Center is part of Providence Brain and Spine Institute.

Providence ALS Center is the leading comprehensive care center in Oregon, certified by the ALS Association as a Center of Excellence offering a multidisciplinary approach to ensure ease and excellence. Our program emphasizes treatment, coordinated care, education and early intervention to manage symptoms.

HEALEY ALS Platform Trial

Description: The HEALEY ALS Platform Trial is a perpetual multi-center, multi-regimen clinical trial evaluating the safety and efficacy of investigational products for the treatment of ALS.

In this trial, multiple investigational products for ALS will be tested simultaneously or sequentially. Each investigational product will be tested in a regimen. Each regimen consists of a placebo-controlled trial, meaning that the active investigational product and matching placebo will be tested in each regimen.

Participants will have an equal chance to be randomized to all regimens that are active at the time of screening. The following regimens are active in the trial: Regimen A - Zilucoplan Regimen B - Verdiperstat Regimen C - CNM-Au8 Regimen D - Priodopidine.

New regimens will be continuously added as new investigational products become available. The HEALEY ALS Platform Trial will enroll additional participants as each new regimen is available.

Sponsor: Merit E. Cudkowicz, M.D.

Radicava® (Edaravone) Findings in Biomarkers From ALS (REFINE-ALS)

Description: Treatment will be prescribed by healthcare providers in accordance with their clinical judgement and the prescribing information for Edaravone. The decision to prescribe Edaravone to the participants should be made separately from the decision to enroll them in the study. There will be no randomized assignments to treatment and no restrictions on the use of commercially available medications (but those participating in an experimental study, even if taking Edaravone, will be excluded). No experimental treatment is evaluated in this study. The intervention is limited to the collection of blood and urine samples for biomarker testing.

During the estimated study period, eligible patients who are prescribed Edaravone within the approved indication will be invited to participate in the study. An initial screening/baseline visit will be scheduled for participants who are considered for study participation.

Participants in this study will be followed from enrollment up to 24 weeks after treatment initiation (6 treatment cycles [each cycle consisting of 28 days], corresponding to a treatment period of approximately 24 weeks) or premature study discontinuation. Throughout the study period, the investigators will record participant baseline and follow-up information and perform clinical and biomarker assessments.

Sponsor: Mitsubishi Tanabe Pharma America Inc.

Therapy in Amyotrophic Lateral Sclerosis (TAME)

Description: ALS is a fatal neurodegenerative disease that affects 30,000 Americans each year. Of these 30,000 Americans, it has been suggested that up to 50% will experience cognitive and behavioral changes in the form of frontotemporal dysfunction and up to 40% will meet criteria for frontotemporal dementia (FTD). Riluzole, the only FDA approved agent for ALS, extends a patient's lifespan by 2-3 months, and there are no proven therapies for the cognitive changes associated with ALS. More effective therapy for this universally fatal disease is desperately needed.

Results from an open label pilot trial of 20 patients treated with memantine at 10 mg BID suggested that treatment with the combination of memantine and riluzole slowed ALS disease progression. This trial also showed that levels of specific protein biomarkers in the CSF at baseline correlated with the rate of disease progression. A concurrent phase II study performed by Dr. Carvalho, found no effect with similar dosing; however, the study was limited in terms of power. Comments on previous failed drug trials in ALS have raised the concern that many ALS trials study a potential therapeutic agent at only a single dose and thus may miss the potential efficacy of non-FDA approved doses; therefore, this proposed study will test a higher dose of memantine, 20 mg BID, in a double blind, placebo controlled, randomized trial of 90 patients with ALS to determine if a therapy of memantine, especially in combination with riluzole, can slow disease progression compared to treatment with riluzole alone or no treatment. The primary outcome measure will be the rate of disease progression as measured by the ALS Functional Rating Scale- Revised (ALSFRS-R). In addition, the investigators will examine the cognitive deficits seen in ALS patients measured by the ALS Cognitive Behavioral Screen (ALS-CBS) and the Neuropsychiatric Inventory Questionnaire (NPI-Q). Finally, the investigators will examine specific validated protein serum biomarkers to determine if there is a correlation between the levels of these biomarkers and the rate of disease progression. In particular, the investigators will measure the ratio of phosphorylated heavy neurofilament to Complement 3 to see if this ratio is predictive of disease progression and if the levels change during therapy with memantine.

Sponsor: University of Kansas Medical Center

Long-Term Evaluation of BIIB067

Description: The primary objective of the study is to evaluate the long-term safety and tolerability of BIIB067 in participants with ALS and confirmed superoxide dismutase 1 (SOD1) mutation. The secondary objectives are to evaluate the pharmacokinetic (PK), pharmacodynamic (PD), and efficacy of BIIB067 administered to participants with ALS and confirmed SOD1 mutation.

Sponsor: Biogen

Evaluation of MN-166 (Ibudilast) for 12 Months Followed by an Open-label Extension for 6 Months in Patients With ALS (COMBAT-ALS)

Description: This is a Phase 2b/3 multicenter, randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy, safety, and tolerability of MN-166 followed by an open-label extension phase compared to matching placebo in subjects diagnosed with ALS.

The study will consist of a screening phase (up to 30 days) followed by a double-blind phase (12 months). Following the screening phase, subjects who continue to meet entry criteria will be randomly assigned to one of two treatment groups: MN-166 or matching placebo in a 1:1 ratio. Upon completion of the double-blind phase, subjects will be given the option to continue to the Open-label Extension Phase for a period of 6 months.

Sponsor: MediciNova

Multiple Doses of AT-1501-A201 in Adults With ALS

Description: This is a Phase 2a, multi-center, open label, multiple dose study of AT-1501, a humanized monoclonal antibody antagonist to CD40LG. Approximately 54 adults with ALS will be enrolled into the study in the United States at up to 12 ALS treatment sites.

Four ascending doses of AT-1501 will be administered as an IV infusion to sequentially enrolling cohorts. Each participant will receive 6 bi-weekly (every other week) infusions of AT-1501 over an 11-week period. The study is estimated to take 19 weeks for participants.

Sponsor: Anelixis Therapeutics, LLC

A Single or Multiple Visit Protocol for Collection of DNA/RNA/Serum/Plasma/CSF in ALS and related disorders

Description: The purpose of this study is to collect DNA, RNA, Serum, Plasma and CSF samples from donors with ALS that will be utilized to delineate vulnerability markers for the disease, enhance the understanding of treatment response and side effects, and develop new targets for future drug development.

This is a single or multiple visit study to evaluate clinical severity and collect DNA/RNA/SERUM/ PLASMA/CSF from donors with ALS and related disorders. Donors will have diagnostic as well as severity evaluating clinical rating scales. Donors who elect to return for additional visits will be seen every 4 months. Study visits consist of administration of rating scales, clinical data, and blood and CSF collection.

Sponsor: PrecisionMed

Clinical Procedures to Support Research in ALS (CAPTURE-ALS)

Description: The purpose of the Clinical Procedures To Support Research (CAPTURE) study is to utilize information collected in the medical record to learn more about ALS and related disorders. The study will consent patients with ALS or related disorders that are receiving care at a clinical center in the CReATe consortium that uses Epic as its electronic health record (EHR) system. The study aims to systematically gather a clinical dataset through the EHR using a standardized approach to characterize the natural history of ALS and related diseases.

Sponsor: University of Miami

Caregiver Interview with Ashley Adamo

Ashley and her husband, Joe, on a backpacking trip around Timberline Trail at Mt Hood.

What is your role at Providence?

I'm the ALS research coordinator. I work closely with Drs. Olney and Bazan to ensure we provide the best care while our patients are enrolled in studies, while acting as a liaison between clinical trial study teams, patients, and our physicians. I perform study assessments like EKGs, muscle testing, questionnaires, and labs, and I manage the data for all the trials.

How did you become interested in ALS and/or clinical research?

My research career began in college during undergraduate. Always a science nerd, I worked on several lab research projects throughout the years. I was also working nights in the ER. When I was going through the "what do I want to do when I grow up" portion of college, a wonderful professor introduced me to the idea of clinical trials. Learning that I could take my passion for caring for others and my drive for science and research and make a career out of it, I knew that was the path for me. Shortly after that, my sister was diagnosed with MS, so that sparked my interest in neurology early on.

There is something special about being on the cutting edge of medicine, but also being able to interact with amazing individuals and provide great care – that's what drew me to join the Providence Research team and work on ALS.

What do you like to do outside of work?

I am an outdoor enthusiast and I love enjoying all that the PNW has to offer – hiking, backpacking, climbing, kayaking, snorkeling, swimming and bodysurfing. My husband and I enjoy camping in remote areas to enjoy nature as much as we can. We have 2 small senior dogs, Leo and Millie, who get most of my attention. I also consider myself to be an amateur chef, since I've watched so many Gordon Ramsey videos over the past year. ■

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