Imaging Biomarker Trial Underway and Seeking More Participants

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Host: ALS Association Chief Scientist Lucie Bruijn, Ph.D.
Guest Speaker: Lyle Ostrow, M.D., Ph.D., By Richard Robinson

An ongoing trial of a new imaging biomarker is looking for participants—that was the message from Lyle Ostrow, M.D., Ph.D., of Johns Hopkins University in Baltimore in a recent webinar sponsored by The ALS Association. Joining the trial offers people with ALS a chance to contribute to the vital effort to develop better ways to track the disease and response to therapy, and it doesn’t exclude people from participation in ALS therapy trials.

“This is not a treatment trial, but its impact on treatment will be tremendous,” said Lucie Bruijn, Ph.D., M.B.A., Association Chief Scientist and host of the webinar.

With funding from The ALS Association, Dr. Ostrow is developing a “positron emission tomography” (PET) imaging marker called 18F-FPEB. This molecule binds to a protein in the central nervous system called mGluR5 (metabotropic glutamate receptor 5). mGluR5 has attracted the attention of the ALS research community because the level of mGluR5 is increased in people with ALS and in animal models of the disease. mGluR5 is involved in handling the neurotransmitter glutamate, and glutamate metabolism is abnormal in ALS, a process which may involve mGluR5.

In PET imaging, a molecule called a ligand (binding partner) is made weakly radioactive, and it injected into the bloodstream. “Wherever it is being used or accumulates, it releases energy, and this can be detected by the PET scanner,” Dr. Ostrow explained. “This allows researchers to make a three-dimensional image of the distribution of the ligand in the body.”

In Dr. Ostrow’s study, the 18F-FPEB ligand will allow him and his colleagues to determine where the mGluR5 protein is in the brain and spinal cord and measure the amount of accumulation. “Our hypothesis is that the density of mGluR5 will be greater in people with ALS than in controls.” The team will look for a correlation between mGluR5 density and disease severity.

“We have a big need for biomarkers in ALS to confirm the diagnosis and to track progression,” he said. Without biomarkers, it can be difficult to interpret data from clinical trials, since a small but significant drug effect can get lost in the “noise” of normal clinical fluctuations.

“Drug companies are highly interested in biomarkers that will shorten clinical trials, and in markers that will determine if a drug is hitting its intended target” said Dr. Ostrow. “If a drug doesn’t get where it needs to go -- and bind to the target and have the effect it should have -- it doesn’t make sense from their perspective to invest in a clinical trial.”
Dr. Ostrow’s study plans to enroll 20 patients, and an equal number of age- and sex-matched controls. Subjects will undergo a screening and MRI session during one visit, and then PET imaging during a second visit.

To be eligible, subjects must have been diagnosed with ALS for more than one but less than three years. The forced vital capacity (FVC) should be less than 80% of predicted, but more than 50% of predicted. Subjects must be able to lie flat for several hours. The MRI takes about 30-40 minutes in the scanner. The PET imaging visit requires 3-4 hours, including 90 minutes in the scanner.

As of late May, Dr. Ostrow has enrolled ten ALS patients and six controls. Spouses are eligible to be controls. Thus far, the procedure is extremely well tolerated with no adverse effects, no complications, and no complaints.

“We hope the data we obtain will allow us to say, ‘Yes, we can do this in ALS patients.’” Future studies will determine if mGluR5 can be tracked over time, and whether it correlates with disease progression. If so, it may offer an important biomarker for future treatment trials.

To participate in the trial, there are no geographic restrictions, but both ALS patients and control participants will need to travel to Baltimore, Maryland for two or possibly three visits – to be examined/screened for inclusion (including lab tests and EKG), receive one MRI scan, and receive one PET scan. Usually the screening exam and MRI can be done on a single day and they would only need to come back one more time for the PET scan. Participants will be paid $300 to help with costs of travel, parking, etc.

To enroll in the trial or to obtain more information, contact Dr. Ostrow by email at Lostrow1@jhmi.edu or call Lora Clawson at 410-955-8511.

Visit https://alsa.webex.com/alsa/ldr.php?RCID=78f711ae72030e8f6ca8826c8a6b9a44 to see the entire webinar.