



\$21 Million Grant Furthers Study into Drug Development for Lewy Body Dementia

There is no approved treatment, but there could soon be hope. Based on some promising initial findings, and a new three-year, \$21 million grant from the National Institute on Aging, researchers at the University of Miami Miller School of Medicine are launching a Phase 2b study of neflamapimod for Lewy Body dementia.



James E. Galvin, M.D., M.P.H.

The multicenter study is a public-private partnership between the Miller School, EIP Pharmaceuticals – the company developing neflamapimod – and the Lewy Body Dementia Association, a non-profit that helps educate the public about the condition and will help promote the study.



Lewy Body dementia (LBD) is a neurodegenerative condition affecting an estimated 1.6 million Americans. Neflamapimod holds potential as a neuroprotective medication if given early enough in the course of LBD, said principal investigator James E. Galvin, M.D., M.P.H., professor of neurology, psychiatry and behavioral sciences, the Alexandria and Bernard Endowed Chair in Memory Disorders, and founding director of the Comprehensive Center for Brain Health at the Miller School.

Dr. Galvin and colleagues plan to randomly assign 160 people with mild-to-moderate LBD to either neflamapimod or a placebo to better understand how the agent works in this population. The investigators will use the Mini Mental State Examination score to help them identify people with mild-to-moderate LBD. They also intend to confirm the safety and efficacy demonstrated in earlier preclinical studies done with mice and subsequent research done with human subjects.

Study participants can be treatment naïve or be taking a cholinesterase inhibitor – a medication commonly prescribed to treat symptoms – but they have to have been taking a stable dose for at least three months.

Protecting LBD-affected Brains

So how could an agent in development like neflamapimod work to protect the brains of people with LBD? A part of the brain called the basal forebrain is where most of the neurons are located that produce a substance called acetylcholine. This neurotransmitter is important for memory, learning, arousal, attention and more. In many neurodegenerative diseases, including LBD, there is a loss of acetylcholine. Without as much acetylcholine, people can start experiencing cognitive



and behavioral symptoms, making it difficult to learn new things, for example.

Loss of acetylcholine happens early in Alzheimer's disease, and perhaps even earlier in LBD, Dr. Galvin said. This makes it an attractive factor to change early on – before people experience worsening symptoms. Neflamapimod works as a very specific inhibitor of an enzyme that leads to loss of brain cells that make acetylcholine. This therapy could work on two fronts, helping to preserve both cognitive function and motor function seen in LBD.

“We don't know for sure whether a drug will or will not work,” Dr. Galvin said, “but pre-clinical data in transgenic mice and cell culture, and data from the Phase 1 and Phase 2a studies, suggest that cognitive function and motor function are likely to show a benefit in patients with Lewy Body disease.”

If neflamapimod is given to someone with the condition after considerable neurodegeneration has already occurred, it may be less likely to help. The researchers will test for levels of a blood biomarker that suggests whether too much degeneration already has occurred for the drug to be protective.

“It seems to be clear from the earlier studies that the people who had the least robust response to the medicine likely were too far advanced in their stage of disease from a pathology perspective,” Dr. Galvin said. “You have to find the right drug for the right person at the right time.”

Right Study, Right Time

He noted that this study is “an ideal opportunity” to partner with industry to test a novel compound like neflamapimod. It's



also the right expertise for the right study at the right time.

“We are one of the top neurology research centers in the country; it’s the perfect opportunity to put together my specific expertise with the rich research environment at the Miller School,” Dr. Galvin said. “The support of the department and the school, the Dean’s office, the CTSI [Clinical and Translational Science Institute] and the research infrastructure really allows us to excel in discovery science and translational science.”

Dr. Galvin also is director and principal investigator for the University of Miami Lewy Body Dementia Research Center of Excellence – one of only 22 such centers in the country and the only one in South Florida.

The FDA already granted the agent fast track status for DLB. If the results of the Phase 2b research are positive, the results could be submitted to the FDA as part of an approval application, and could help inform a larger, Phase 3 study.

For more information on the study, email healthybrain@miami.edu.

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