

FAU to host potentially groundbreaking drug trial for Lewy body disease



The double-blind trial will examine the effects of RVT-101, which stimulates the release of acetylcholine in the brain, on a total of 240 patients diagnosed with dementia with Lewy bodies, said Axovant officials. Results are expected in 2017, with the medication coming to market in 2018 if all goes well.



By **Diane C. Lade · Contact Reporter**
South Florida Sun-Sentinel

FEBRUARY 28, 2016, 5:45 PM

South Florida will be part of potentially groundbreaking research into a little-known, but not uncommon, neurological disorder that is often misdiagnosed as Alzheimer's disease.

The first U.S. clinical trial to look at medications targeting what's termed "dementia with Lewy bodies" will include a site at Florida Atlantic University in **Boca Raton**. The disease has no specific treatment or cure.

Patient enrollment is expected to begin in March.

Dr. James Galvin, a professor and associate dean for clinical research at FAU's Charles E. Schmidt

College of Medicine who will head the South Florida trial, called Lewy body "the most common disease you've never heard of" — even though about 1.3 million Americans have it.

One of them was actor-comedian Robin Williams, who was 63 when he killed himself in August 2014.

An autopsy showed that Williams had the abnormal Lewy body protein deposits in his brain. His family said he began showing symptoms in November 2013. Within six months, the A-list entertainer had a shuffling gait, was losing his voice, and was slipping in and out of reality, his widow, Susan Williams, told ABC's "Good Morning America" in November.

Lewy body is the second most-common dementia after the far better-known Alzheimer's, and the two often overlap. About 80 percent of all patients with Lewy body also have Alzheimer's, Galvin said, and 40 percent of all Alzheimer's patients have Lewy body as well. The disease also can co-exist with Parkinson's.

While all three diseases have similar causes and symptoms — they typically are age-related, irreversible, and dreaded by seniors and their families — Lewy body in some ways is particularly brutal, experts say. Lewy body patients tend to be younger than those with Alzheimer's, deteriorate more quickly and develop extreme symptoms like hallucinations and violent nightmares early in the disease process.

They often resemble Parkinson's patients, Galvin said, with a shuffling walk, stiffness and balance problems. While Alzheimer's patients typically have gradual but steady declines in memory and cognition skills, the ability to concentrate and stay in reality can fluctuate drastically among Lewy body patients, Galvin said.

Because its symptoms mimic other diseases, physicians can find it difficult to recognize Lewy body dementia, Galvin said. In some cases, patients are told they have a psychiatric problem like bipolar disorder, he said.

"Most diagnoses take about 18 months, with patients seeing six physicians over multiple visits," said Galvin, a nationally known Lewy body expert.

Families are even less likely to recognize the disease. Cosimo Avella, of West Palm Beach, realized something was wrong almost four years ago when his mother, who loved preparing meals for their large extended Italian family, started over- or under-cooking the food and setting the table for people who were not there.

"In the beginning, I felt like, my God, I have lost my mom, there's nobody home," said Avella, 29, a paramedic and guard for a security company.

Raffaella Avella was 69 when she was diagnosed with Lewy body six months later.

The only way to definitively determine whether someone has Alzheimer's or Lewy body is through a post-mortem brain autopsy. An incorrect diagnosis can be disastrous. Lewy body patients can have severe adverse reactions to medications commonly used to treat the symptoms of Parkinson's, Alzheimer's and psychiatric disorders.

Raffaella Avella initially was on several medications, including one for Parkinson's-like issues, that made her hallucinate wildly.

"She constantly was talking to pillows and lamps and people who were not there," Cosimo Avella said. "So we slowly weaned her off the meds, and the hallucinations stopped."

Today, his mother's condition is much more stable. Cosimo Avella is grateful she's able to visit a Wellington day care center run by the nonprofit Alzheimer's Community Care service agency, based in West Palm Beach.

"I know there is nothing that can bring her back to who she was, but we have figured out a system that works for her," he said.

Lewy body disease is named for scientist Friederich H. Lewy who in the early 1900s discovered abnormal protein deposits — which became known as "Lewy bodies" — in the brain. Those proteins can deplete the neurotransmitter dopamine, causing physical symptoms like stiffness and balance loss, and the brain chemical acetylcholine, which affects memory and behavior.

Currently, Lewy body patients often are treated with drugs designed for Alzheimer's disease. The HEADWAY-DLB (dementia with Lewy bodies) study, being conducted by Bermuda-based Axovant Sciences at FAU and up to about 50 other sites worldwide, is the first in the United States aimed at bringing a new drug to market specifically for this disorder, Galvin said.

The double-blind trial will examine the effects of RVT-101, which stimulates the release of acetylcholine in the brain, on a total of 240 patients diagnosed with dementia with Lewy bodies, said Axovant officials. Results are expected in 2017, with the medication coming to market in 2018 if all goes well, said Dr. Larry Friedhoff, Axovant's chief development officer.

FAU probably will enroll 10 to 16 patients, Galvin said. They will be paid for their time and expenses.

Axovant started out testing RVT-101 on Alzheimer's patients in its MINDSET study, now in phase three of the four-stage clinical trial process. Participants in the Lewy body study will be given higher RVT-101 doses than those in the Alzheimer's trial, Friedhoff said.

The company also has another study in the pipeline looking at the drug Nelotanserin as a treatment for patients with Lewy bodies or Parkinson's dementias who have hallucinations.

"A lot of people are pessimistic about our chances of success," Friedhoff said, as clinical trials for new drugs aimed at neurodegenerative dementias repeatedly have failed for more than a decade, dashing hope. "But I think we have about as strong of a case as we can for these drugs helping patients."

Looking to speed up the diagnostic process and reduce risks like medication interactions, Galvin developed a three-minute screening test that primary care doctors, nurses and social service professionals can use to help determine whether someone might have Lewy body and need to see a neurologist. The Lewy Body Composite Risk Score screen is a list of 10 questions about physical signs or behaviors. More than two "yes" answers indicates Lewy bodies might be involved.

"The idea was to take what we know and create a tool that people could use easily," Galvin said.

He began studying the disease in 1993, after watching his grandfather struggle with the condition.

Galvin's study of 265 patients — published last year in "Alzheimer's and Dementia," the national Alzheimer's Association's journal — suggests the test could discriminate between Lewy body and Alzheimer's almost 97 percent of the time.

Primary care doctors who can quickly and accurately identify Lewy body disease also can better prepare families for what could be a faster and more serious decline in their loved one's health than they might expect, said Dr. Naushira Pandya, director of the Geriatric Education Center at Nova Southeastern University's College of Osteopathic Medicine.

"It's easy to miss the disease in its early stages," Pandya said. "As soon as a doctor suspects it, it's time to start asking: Who will make medical decisions for the patient? Where will they live? Families need to plan not only logistically but financially. There is no cure."

Patients diagnosed with dementia with Lewy bodies can enroll in the HEADWAY-DLB study by calling coordinator Katty Savaria at 561-297-4802.

dlade@tribpub.com or 954-356-4295