

## Case Western Reserve University researchers use skin cancer drug to reverse Alzheimer's symptoms in mice

By Brie Zeltner, the Plain Dealer, [blog.Cleveland.com](http://blog.Cleveland.com)

Case Western Reserve University researchers have found what may be a new treatment for early-stage Alzheimer's disease. The drug rapidly clears out the sticky plaques that build up in the brains of those with the disease and improves memory and thinking.

But they caution that their stunning results -- total plaque clearance and symptom improvement in a short 72 hours -- need to be put in perspective: They've only tested the drug -- an already approved cancer medication called **bexarotene** -- in mice. It may be years before the treatment is ready for people, *if* it proves to work the same way in human trials.

**Alzheimer's disease**, the most common cause of dementia, affects 5.4 million Americans and is newly diagnosed every 69 seconds, according to the **Alzheimer's Association**. There is no cure, and the few available treatments do nothing to stop its progression.

Perhaps the best news about the Case research is that bexarotene is already FDA-approved for the treatment of cutaneous T-cell lymphoma. That should cut about a decade out of the drug's development for Alzheimer's if all goes well, said **Gary Landreth**, professor of neurosciences at Case and senior author on the paper that outlined the results.

Landreth and his team published their **results** online today in the journal **Science**.

Landreth said they were stunned by how quickly the drug did its work in the brains of mice that are bred to mimic the Alzheimer's condition.

"It was extraordinarily effective," he said. "We had one of these 'gee whiz' moments. We actually couldn't believe how effective this drug was."

After only three days, the drug cleared out the amyloid beta protein plaques that many researchers believe are central to the disease. It also lowered the level of the forms of the protein that circulate freely in the mouse brains.

Amyloid beta is cleared from the brain by apolipoprotein E, a protein regulated by a gene called ApoE. The gene-protein-amyloid process has long been a target of drug treatments for Alzheimer's, and Landreth's team has been researching ways to quickly clear amyloid beta from the brain for the past decade.

There are also two vaccine treatments, which would use the body's immune system to protect against the overproduction of the amyloid protein and its buildup, currently in Phase III trials. Those treatments take about six months to clear plaques from the brain in mice, Landreth said.

But is faster better? That's hard to tell right now, he said, and the question is a source of some trepidation.

"The thing that's kind of scary about this is that the drug is so effective at pulling plaque out of the brain, at least in mice, that if it does a similar thing in humans we don't know what will happen," Landreth said. "This is brand new stuff. We think it might not be a good idea to rapidly change structural elements in your brain."

They also don't know if the drug will do anything for people who have more advanced Alzheimer's disease, which usually involves brain cell death. The mouse models they work with can't mimic that part of the disease, so there's no way to tell.

"We're not going to answer that question until we go to human [trial]s," he said.

For now, his team is moving ahead with a trial that will determine if the drug works the same way in healthy people as it does in mice. They hope to start within two months, and the trial should take four months to complete.

After that, "we're off in Never Never Land -- we don't know," he said.

One of the problems they face is funding. The patents for bexarotene, marketed by the pharmaceutical company **Eisai, Inc.** under the trade name **Targretin**, will expire starting this year and the drug company has shown no interest in funding studies, he said.

That leaves government and private funding.

Because the need is so great, Landreth and his team feel a sense of urgency in moving the research forward. But, he made one point very clear: even though you theoretically can get the drug from a doctor today, it's not ready for human use in Alzheimer's patients.

"I'd like to say very loudly and clearly, don't try this at home," he said, noting that the doses they used in the study were the FDA-approved cancer treatment strength, and are likely much too high.

"There's going to be an opportunity for doctors to prescribe this off-label. And at the moment that's a very dangerous proposition because we don't know how to optimally deliver the drug. We can't advise anyone taking this drug for their Alzheimer's until we figure it out."