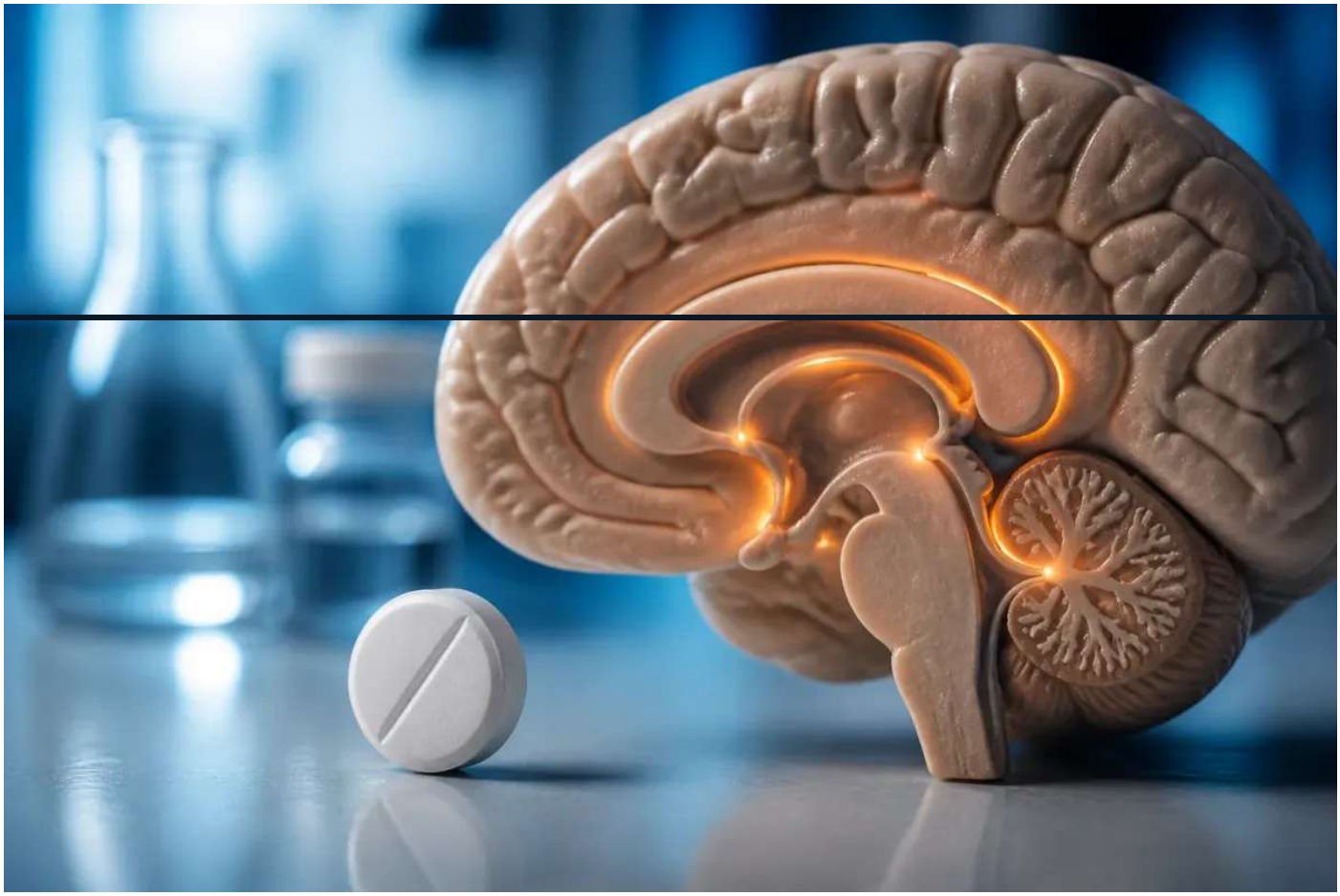
Cortisol-blocking pill shows mixed results in Alzheimer's trial

Xanamem did not deliver a statistically significant benefit across a 247-person Alzheimer's trial, although an analysis of participants older than 75 suggested slower disease progression. A larger follow-up study is planned.

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A once-daily pill designed to reduce cortisol production in the brain has produced mixed results in a clinical trial involving 247 people with mild to moderate Alzheimer's disease. The treatment, known as Xanamem, failed to show a statistically significant benefit across the full study population. However, participants older than the trial's median age of 75 reportedly experienced a 30 per cent slowing of disease progression after 36 weeks.

The result offers a possible signal of benefit for older patients, but it does not establish that the drug is effective. Findings from a subgroup can help researchers decide what to test next, particularly when a trial's overall result is negative, but they require confirmation in a larger and appropriately designed study. Actinogen, the Australian biotechnology company developing Xanamem, expects a follow-up trial involving 700 patients to begin in the middle of the following year.

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What the trial found

The double-blind, placebo-controlled trial was conducted in Australia and the United States. Participants received either a 10 milligram dose of Xanamem or a placebo each day for 36 weeks. All had mild to moderate Alzheimer’s disease, placing the study’s focus on people whose illness had already progressed beyond its earliest stage.

Across all 247 participants, the difference between the treatment and placebo groups did not reach statistical significance. That is the trial’s central outcome and an important limitation when interpreting the more encouraging result among older participants. About half the study group was above the median age of 75, and Actinogen reported that disease progression in this subgroup slowed by 30 per cent by the end of treatment.

Actinogen chief executive Dr Steven Gourlay said the company was disappointed that a similar benefit was not observed in younger participants. He suggested the stronger signal in older patients could be associated with inflammation, noting that older people may have higher inflammatory markers. That remains a proposed explanation rather than a conclusion demonstrated by the reported trial findings.

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The company believes an oral, low-dose treatment could have practical advantages over some existing therapies, including lower cost and fewer side effects. Those potential advantages have not yet been established through the information reported from this study. Safety, effectiveness and cost would all require fuller evidence and regulatory assessment before the medicine could become routinely available.

Why Xanamem targets cortisol

Xanamem, whose active compound is emestedastat, is intended to block cortisol production in brain regions associated with Alzheimer's progression. Cortisol is a necessary hormone involved in the body's response to stress, but the drug's underlying hypothesis is that persistently elevated levels can become harmful to neurons.

Research has linked high cortisol with cognitive decline and other illnesses. Prolonged elevation has also been associated with the development of amyloid beta plaques, one of the characteristic changes seen in Alzheimer's disease. Professor Michael Woodward, an honorary medical adviser to Dementia Australia, said cortisol is important in dementia and that blocking it may help prevent some changes associated with Alzheimer's.

This mechanism differs from recently introduced monoclonal antibody treatments such as donanemab and lecanemab. Those medicines act on amyloid beta plaque in the brain. Other experimental approaches target tau, an abnormal protein that can form tangled clumps inside brain cells and interfere with communication and cellular transport. Researchers continue to debate the relative roles of amyloid, tau and other biological processes in driving the disease.

Gourlay compared the reported 30 per cent slowing in the older subgroup with reductions of between 22 and 27 per cent attributed in the source report to recently approved antibody treatments. The figures cannot by themselves establish that Xanamem performs as well as those medicines: they come from different trials, patient groups and treatment designs, while Xanamem's overall trial result was not statistically significant.

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A field testing several approaches

The Xanamem findings arrive amid broader efforts to develop treatments and diagnostic tools for Alzheimer's disease. Australia approved disease-modifying antibody drugs and a blood test for diagnosis in the previous year, according to the report. These developments represent movement after decades in which researchers struggled to produce therapies capable of interfering with the underlying course of the illness.

A separate University of Sydney project has tested experimental mRNA-based nose drops in mice carrying genetic mutations associated with Alzheimer's. Researchers reported that the drops prevented cognitive decline and memory loss in the animal model. The nasal approach is intended to bypass the blood-brain barrier, which can prevent medicines from reaching the brain.

Those nose-drop findings remain preclinical. Results in genetically modified mice do not show that a treatment will be safe or effective in people, and human trials are the stated next step. The project is therefore at a different stage from Xanamem, which has already been administered to patients but still needs stronger evidence of benefit.

What happens next

The planned 700-person Xanamem trial will be important for determining whether the apparent effect in older patients can be reproduced. It may also help clarify which patients, if any, are most likely to benefit, as well as the treatment's safety profile and the durability of any effect. Actinogen hopes to bring the drug to market in 2030, but that ambition depends on future trial outcomes and the relevant approval processes.

For now, the evidence supports cautious interest rather than a conclusion that a new Alzheimer's treatment has been proven. The negative overall result and positive older subgroup point in different directions, making confirmation essential. Mixed trial findings are common in dementia research, and subgroup results are most useful when they generate a clear question for a subsequent study.

The original reporting is available from **Clair Weaver at The Age (https://www.theage.com.au/lifestyle/health-and-wellness/daily-pill-to-block-cortisol-offers-hope-for-older-people-with-dementia-20261119-p61ehb.html)**. For additional coverage of medical research and public health, visit **2minutes.news Health (https://2minutes.news/en/health)**.

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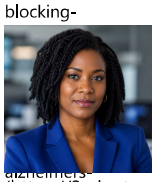
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