Medical Xpress

Evidence of sustained benefits of pimavanserin for dementia-related psychosis

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Evidence of the sustained benefits of an investigational antipsychotic treatment for people with dementia-related psychosis has been published.

Up to half of the 45 million people worldwide who are living with

Alzheimer's disease will experience psychotic episodes, a figure that is even higher in some other forms of dementia. Psychosis is linked to a faster deterioration in dementia.

Despite this, there is no approved safe and effective treatment for these particularly distressing symptoms. In people with dementia, widely-used antipsychotics lead to sedation, falls and increased risk of deaths.

Pimavanserin works by blocking serotonin 5HT2A receptors, and doesn't interact with the dopamine receptors. It is licensed in the US to treat hallucinations and delusions in people with Parkinson's disease psychosis.

A new paper published in the *New England Journal of Medicine* outlines a clinical trial, conducted in 392 people with psychosis associated with Alzheimer's disease, Parkinson's disease, Lewy body, frontotemporal, or vascular dementia. All participants were given pimavanserin for 12 weeks. Those who met a threshold of symptom improvement were then assigned to pimavanserin or placebo for up to 26 weeks.

The trial was stopped early for positive efficacy results. Of the 351 participants, 217 (61.8%) had a sustained initial treatment benefit, of whom 112 were assigned to placebo and 105 to pimavanserin. Relapse occurred in 28/99 (28.3%) of the placebo group, compared to 12/95 (12.6%) of the pimvanserin group, with pimvanserin more than halving the relapse rate and significantly improving the sustained benefit.

Professor Clive Ballard, Executive Dean of the University of Exeter Medical School, said: "Psychosis affects up to half of all people with dementia, and it's a particularly distressing symptom—yet there's currently no safe and effective treatment. Currently used antipsychotics are known to cause harms, and best practice guidelines recommend prescribing for no longer than 12 weeks for people with dementia as a

result. We urgently need alternatives. It's exciting that the relapse rate in the pimavanserin group was lower than the placebo group, indicating that the treatment benefits may be sustained over time. We now need longer and larger scale trials to explore this further."

The trial found headache, urinary tract infection and constipation occurred more frequently in the pimavanserin group, but there was no increase in mortality or the other serious events, such as stroke, which are known to increase with other antipsychotics.

The full paper is entitled "Trial of Pimavanserin in Dementia-related psychosis," published in the *New England Journal of Medicine*.

More information: Pierre N. Tariot et al, Trial of Pimavanserin in Dementia-Related Psychosis, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMoa2034634

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