Medical Xpress

# New drug could offer first safe and effective treatment for psychotic symptoms

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Up to 10 million people worldwide have Parkinson's disease and more than 50 percent of them will experience psychosis (mainly hallucinations and delusions) at some time. Pimavanserin, a new non-dopaminergic drug, may offer the first safe and effective treatment for these psychotic symptoms, according to a phase 3 randomized trial published in *The Lancet*.

"Psychotic symptoms are common and distressing for people with Parkinson's and those caring for them. Psychosis is a major driving factor for people with Parkinson's disease being admitted to nursing homes and substantially increases the risk of dying. But no safe and effective drug therapies exist", explains study leader Professor Clive Ballard from King's College London, UK.

"Currently, the only treatment options are dopamine antagonist antipsychotic drugs such as clozapine and quetiapine which worsen motor symptoms, speed up cognitive decline, increase the risk of stroke, and can be life-threatening even with short-term use."

Pimavanserin works by blocking serotonin 5-HT2A receptors in the neocortex (the part of the brain responsible for sensory perceptions, conscious thought, and language) that are associated with visual hallucinations and delusions.

In this study, Ballard and colleagues recruited 199 patients with Parkinson's disease psychosis, aged 40 years or older, from 54 centres

across the USA and Canada. Participants were randomly assigned to receive 40mg of pimavanserin orally once daily or matching placebo for 6 weeks. A nine-item Parkinson's disease-adapted scale (SAPS-PD) was used to assess positive symptoms of psychosis at the start of the study and at regular intervals up to day 43.

The researchers used a brief run-in phase of psychosocial interaction to reduce the common placebo effect noted in Parkinson's disease clinical trials when treatment starts.

After 43 days, patients taking pimavanserin showed a significant improvement in SADS-PD score (psychotic symptoms) compared with those given placebo (37% improvement vs 14%). Additionally, improvements in night-time sleep, daytime wakefulness, and caregiver burden were also noted compared with placebo. No worsening of motor symptoms was reported in patients given pimavanserin.

Importantly, says Professor Ballard, "The clinical benefits of pimavanserin were seen by patients, those caring for them, and independent blinded raters alike."

Pimavanserin was generally well tolerated, and treatment-related adverse events were mild to moderate and similar between the two groups. The most common were urinary tract infections (12% placebo vs 14% pimavanserin) and falls (9% vs 11%). Ten patients discontinued taking pimavanserin because of an adverse event compared with four in the placebo group.

Based on these results the researchers suggest that pimavanserin also has the potential to be used to treat psychotic symptoms common in Alzheimer's and other dementias.

Writing in a linked Comment, Susan Fox an Associate Professor of

Neurology at the University of Toronto in Canada says, "Further studies will be needed to determine relative efficacy of pimavanserin and clozapine or quetiapine…[but] Overall, the study opens up a new therapeutic avenue in treatment of Parkinson's disease psychosis. With a potentially improved safety profile, pimavanserin might be useful for treatment of patients with Parkinson's disease and mild symptoms of psychosis and help prevent progression to more bothersome symptoms as well as targeting psychosis in other disorders such as Alzheimer's disease."

**More information:** www.thelancet.com/journals/lan … (13)62106-6/abstract

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