

Non-dopaminergic drug preladenant reduces motor fluctuations in patients with Parkinson's disease

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Preladenant, a non-dopaminergic medication, reduces off time in patients with Parkinson's disease receiving standard dopamine therapy, an international study led by the University of South Florida found.

Results of the double-blind, [randomized clinical trial](#) are reported online today in the journal *Lancet Neurology*. The findings suggest that preladenant may offer a new supplemental treatment for Parkinson's disease without some of the complications of levodopa and other standard [dopamine](#) treatments.

"The goal of treatment is to provide the best possible function and quality of life to patients over time," said lead author Dr. Robert A. Hauser, director of the Parkinson's Disease and Movement Disorders Center at USF. "After a few years, many patients find that their traditional Parkinson's disease medications wear off after a few hours leading to a re-emergence of symptoms. In this study, preladenant was shown to reduce off time, thereby affording patients more time through the day with better function."

Dr. Hauser and colleagues evaluated the safety and effectiveness of a range of doses of preladenant in 253 patients experiencing "wearing off" symptoms from their levodopa therapy. The patients were also receiving other available anti-parkinsonian drugs, such as dopamine agonists and/or entacapone.

The 12-week study found that the addition of 5 and 10 mg of praladenant twice daily significantly reduced "off time" -- the re-emergence of troublesome motor symptoms such as slowness, stiffness, tremors, and immobility – when compared to patients receiving similar doses of placebo. Furthermore, praladenant significantly increased "on time" – the period during which patients' Parkinson's symptoms were adequately controlled --.without significantly worsening dyskinesia (involuntary twisting, turning movements). The doses were well tolerated, and the incidence of treatment-related adverse effects was similar for patients receiving praladenant and placebo.

In Parkinson's disease, the brain's dopamine-producing cells falter and die, leading to movement-related or motor symptoms such as tremors, stiffness, slowness, and balance problems.

Levodopa, a compound converted into dopamine in the brain, is still the gold standard therapy for Parkinson's, but as the disease advances this standard drug works for increasingly shorter time periods. As a result, patients begin to experience impaired movement before their next scheduled dose of medication. The re-emergence of symptoms accompanying this "off-time" can make it difficult for patients to perform even the most basic functions, such as walking and dressing. In addition, over time patients tend to develop a sensitivity to levodopa therapy during "on-time" resulting in involuntary twisting, turning movements known as dyskinesia.

Currently available drugs widely used to treat [Parkinson's disease](#) correct for the loss of the neurotransmitter dopamine – either by boosting available dopamine in the brain or directly stimulating dopamine receptors. New ways to treat the disease that better address motor fluctuations without adverse side effects continue to be sought. Praladenant is a non-dopaminergic medication that targets adenosine A2A receptors in the motor control areas of the brain. It may offer

advantages over dopamine medications, possibly including fewer side effects.

The clinical trial was conducted at 44 sites in 15 countries. Preladenant is an investigational medicine and is not approved for use.

Provided by University of South Florida

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