Accordion Pill May Help Reduce Motor Fluctuations in Parkinson's Disease, Phase 2 Trial Shows

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The Accordion Pill Carbidopa/Levodopa (AP-CD/LD) administered three times a day reduced the variability of blood plasma levels of levodopa in Parkinson's disease patients, which suggests that the treatment may help to ease motor fluctuations, a Phase 2 trial shows.

Warren Olanow, MD, professor at Mount Sinai School of Medicine, New York, and the study's lead author shared these results in a scientific poster, titled "Pharmacokinetics of multiple doses of Accordion Pill Carbidopa/Levodopa in patients with Parkinson's disease," at the *2019 IAPRD World Congress*, June 16–19 in Montreal, Canada.

Levodopa is the most widely used treatment for Parkinson's motor symptoms, and is almost always given in combination with carbidopa — a molecule that ensures levodopa is safely delivered to the brain, where it is processed to generate dopamine. Low levels of dopamine in Parkinson's patients lead to the characteristic motor impairments associated with the disease.

However, patients with advanced disease who are being treated with levodopa often develop motor fluctuations, which result from "off" periods (when symptoms return) between levodopa doses due to its short-term effects.

This limited effectiveness is associated with the restricted absorption of levodopa in the upper part of the gastrointestinal tract, meaning that it has a short period of absorption.

Intec Pharma's AP-CD/LD was designed to address this problem. The pill has a specific gastric retention and release system containing carbidopa and levodopa which allows the therapy to be released in both immediate and controlled-release modes.

Controlled release enables a slow discharge of the therapy in the stomach over eight to 12 hours, potentially allowing for more steady absorption in the upper gastrointestinal tract, where levodopa is absorbed.

The Phase 2 study (NCT03576638) evaluated the pharmacokinetic (PK) profile (a compound's processing inside the body) of AP-CD/LD compared to Sinemet (an approved combination of immediate-release carbidopa-levodopa, marketed by Merck) in 12 Parkinson's patients.

Participants received either an AP-CD/LD capsule — containing 50 mg of carbidopa with 500 mg of levodopa — three times a day, or they were given an immediate-release Sinemet tablet — consisting of 37.5 mg of carbidopa and 150 mg of levodopa — five times a day.

Blood samples were collected pre-dose, and then at 30-minute intervals post-dose over 16 hours and again at 24 hours post-dose.

The study's main objective was to assess the variability in the blood concentration of levopoda between four and 16 hours after dosing.

The results showed that patients treated with AP-CD/LD three times a day had less variability in the concentration of levopoda in their blood compared with those given Sinemet given five times a day. Treatment with AP-CD/LD was found to be safe as there were no reports of adverse events.

As decreasing the fluctuations in blood levopoda levels is linked with reduced motor complications, "these preliminary results suggest that treatment with AP-CD/LD may reduce motor complications compared with standard [immediate-release]-CD/LD treatment in advanced [Parkinson's disease] patients," the researchers wrote.

"These PK results are important as they confirm our expectations that AP-CD/LD 50/500 [three times per day] reduces levodopa variability in [Parkinson's disease] patients, which we expect will translate to a reduction in motor fluctuations in these patients," Jeffrey A. Meckler, vice chairman and CEO of Intec Pharma said in a press release.

Intec Pharma is also conducting a Phase 3 trial, named ACCORDANCE (NCT02605434), to compare the safety and efficacy of AP-CD/LD and Sinemet in hundreds of adults with advanced Parkinson's.

"We are eagerly awaiting the top-line results from our Phase 3 ACCORDANCE trial in the July/August time frame and these positive PK data support our belief that AP-CD/LD treatment could provide Parkinson's disease patients with a better baseline [levodopa] therapy to reduce motor complications," Meckler added.