A New Long-Acting Carbidopa/Levodopa Formulation

Michael Rezak, MD, PhD, Parkinson’s Disease Research Society (from www.APDAparkinson.org), originally released April 15, 2013

Rytary™, although not yet released, has been shown to be effective in treating both early and later stage Parkinson’s disease symptoms. It is a unique formulation of carbidopa/levodopa, which provides longer and more stable duration of action compared to immediate release carbidopa/levodopa or even carbidopa/levodopa with comtan (Stalevo®). Rytary™ capsules are manufactured so that they contain beads that release carbidopa/levodopa at different rates as they dissolve, thereby allowing absorption in the gastrointestinal tract over a prolonged period of time. At the same time, this may mean that higher total doses of levodopa are required to achieve the same blood levels achieved by more immediate release formulations. Rytary™ has been shown to benefit both early PD symptoms and reduce OFF time in patients that are experiencing “wearing off” phenomenon.

In moderate to advanced PD patients that were experiencing motor fluctuations, Rytary™ demonstrated about 2 hours per day of reduced OFF time, improved quality of life measures and patients rated themselves significantly more improved compared to taking the immediate release carbidopa/levodopa formulation. Nevertheless, dyskinesias remained a problem. Another study looking at Rytary™ in more advanced fluctuating patients compared to those taking Stalevo® (carbidopa/levodopa/entacapone) demonstrated about 1.5 hours of reduced OFF time as well as a reduction in dosing frequency from about 5.5 times per day to 3.5 times per day. In early Parkinson’s disease, Rytary™ provided a clear symptomatic benefit. The higher the dose, the greater the improvement in motor symptoms and activity of daily living compared to placebo, but side effect frequency also increased as the doses were escalated. It is expected that the dosing frequency should be three times per day for most early PD patients and may be reduced to around 2/3 of the current dosing frequency in more advanced patients.

Several important questions remain with regard to Rytary™ in early PD. First, is whether Rytary™ will turn out to be more effective for symptoms than immediate release carbidopa/levodopa and will there be fewer side effects—the answer awaits further studies. Secondly, the key question of whether using a truly longer acting, less pulsatile formulation of carbidopa/levodopa reduces the likelihood of developing motor complications and dyskinesias—this answer also awaits future studies.

We look forward to finally having an oral long-acting carbidopa/levodopa formulation that has the potential to allow use earlier in the course of PD. It is now well established that the short half-life of immediate release carbidopa/levodopa (60-90 minutes) is a major factor in the development of motor fluctuations and dyskinesias. Thus, Rytary™, with its more stable and continuous distribution (half-life of about 4 hours), may have the capacity to reduce the probability of developing motor complications in PD with levodopa use.

For now, the strategy for most Parkinson’s specialists remains that levodopa use be delayed until it is needed. Utilizing a polypharmacy approach by employing other medications (Azilect®, Neupro®, Mirapex®, Requip®, amantadine, etc.) before turning to l-dopa remains the overall guiding principle in our effort to forestall motor complications. It is possible that this strategy may change if studies demonstrate that Rytary™ has a lower propensity to result in motor complications.

In moderate to advanced PD, reduced dosing frequency and more ON time is a highly desirable benefit of Rytary™, but dyskinesias will probably remain problematic, at least in patients who had been using short acting levodopa prior to Rytary™.

Parkinson’s Data Collection Bill Introduced
Parkinson’s Action Network, January 14, 2015

The Parkinson’s Action Network (PAN) is excited to announce that the Advancing Research for Neurological Diseases Act of 2015 has been introduced by Rep. Michael C. Burgess (R-TX) and Rep. Chris Van Hollen (D-MD). The bill will create a data collection system at the Centers for Disease Control and Prevention (CDC) on Parkinson’s disease, multiple sclerosis, and other neurological disorders.

This system at the CDC would provide data on the epidemiology, incidence, and prevalence of this progressive, neurodegenerative disease. Better data would allow for future planning of health care needs, detect changes in health practices, assess disease burden, promote education about neurological diseases, and support a wide range of research initiatives.

Now, PAN needs your help to ensure this legislation gets support in the House.

Ask your Representative to co-sponsor H.R. 292, the Advancing Research for Neurological Diseases Act of 2015! Take Action!
February Membership Meeting

Saturday, February 21 ■ 2:00 p.m.
Medical Office Building, St. David’s Medical Center
5th Floor Conference Room, 3000 N. IH-35

Dr. Stanley Fisher will be speaking on “Living Well with PD: Understanding Parkinson’s Disease and Current Treatments.” Dr. Fisher is the Founder and Co-Director of the Movement Disorders and Neurorehabilitation Center at Methodist Neurological Institute and Associate Professor of Neurology at Weill Cornell Medical College. He combined his skills as a robotic engineer, fitness trainer and neurologist to do research in the use of robotically-assisted technology for neurological rehabilitation and became a nationally recognized expert in the field of Neuromodulation, utilizing implantable devices for the treatment of Parkinson disease, tremor, dystonia, as well as spasticity due to stroke, multiple sclerosis, traumatic brain and spinal cord injury. Dr. Fisher is involved in clinical research related to psychosis and emotional lability in patients with neurodegenerative disorders and has a strong interest in the field of Targeted Drug Delivery in the treatment of pain and neurological diseases.

Our program is followed by a potluck meal. Your contributions are appreciated.