NEW TREATMENT ADVANCES IN EARLY PD

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Today there are evidences that starting the treatment of Parkinson's disease as soon as symptoms emerge may be beneficial for the patients. Levodopa remains the most effective treatment of PD but the risk of developing motor complications remains the main problem for its early use. In the early stage may be convenient to start with a MAOB inhibitor like rasagiline. This drug proved to be effective in monotherapy the early stage of the disease.

Dopamine agonists are still the first line treatment but they have to be administered three times per day and may produce side effects moreover the benefits of DA-agonist monotherapy in early PD patients are reduced over 2-3 years. Addition of L-dopa, a common practice, leads to motor fluctuations and potentially, dyskinesias.

To overcome the problem of multiple daily administrations and after a more continuous dopaminergic stimulations different mode of administration have been tested.

A prolonged-release formulation (ropinirole 24-hour prolonged release) that provides 24-hour exposure from a single daily dose has been developed. Once daily dosing of this prolonged-release formulation should provide a much more convenient dosing regimen, a simpler dose titration and potentially a more rapid attainment of an effective treatment dose compared with the immediate-release formulation. Preliminary data suggest that ropinirole 24-hour prolonged release has a smooth pharmacokinetic profile with a slower rate of absorption and more consistent plasma drug levels throughout the day than ropinirole immediate release, and with a slower rate of rise to C_{max} when starting therapy and during titration. This compound proved to ensure the same efficacy than ropinirole IR in a double blind cross over study in early patients. Another new way of administration is the transdermal delivery-using patch. Rotigotine is a novel dopamine agonist with good transedermal absorption. This compound proved to be efficacious in patients with early Parkinson's disease and can represent a valid alternative to oral treatments. Another dopamine agonist, lisuride, has been tested as a patch but only in fluctuators.

There is also study exploring the possibility of prolonging dopamine agonist therapy avoiding the use of levodopa.

Safinamide, a new selective and reversible MAO-B inhibitor, that inhibits dopamine re- uptake and glutamate release, and does not potentiate the effects of tyramine has shown clinically and statistically significant efficacy as an add-on to a stable dose of a DA-agonist in a previous Phase 2 trial.

In another study safinamide 50-100mg/day and 150-200mg/day was administered in 270 parkinsonian patients with < 5 years of disease, who had not received L-Dopa previously and were on a stable dose of a single DA-agonist for at least 4 weeks prior to baseline.

Analysis of efficacy indicates that Safinamide 50-100 mg/day was significantly superior to placebo on the mean change and responder (≥ 30% improvement) analyses of the UPDRS III, CGI-C responders (score of 1, 2 or 3), UPDRS II, EuroQoL and on the Cogtest battery that was specially designed to evaluate cognitive domains known to be impaired in PD patients.

Moreover there are study to test new way to deliver levodopa in early PD. It may be possible that changing the way of levodopa administration in the early stage of disease may limit the development of motor complications.