Open-Label Extension to the Double-Blind SP512 Trial to Assess the Safety of Long-Term Treatment of Rotigotine in Subjects with Early-Stage Idiopathic Parkinson’s Disease

Background
- The development of motor complications in patients with Parkinson’s disease (PD) is associated with prolonged stimulation of dopamine receptors, especially when using short-acting dopaminergic agents.1
- Prolonged stimulation due to fluctuating plasma levels of orally administered dopamine agonists may limit the long-term effectiveness of these drugs.2
- Rotigotine® is a unique dopamine agonist with activity across D1 through D5 receptors as well as select adrenergic and serotonergic sites;3 continuous, steady transdermal delivery maintains stable plasma levels over 24 hours with a single daily application.
- In a 6-month, randomized, double-blind, placebo-controlled trial, rotigotine was shown to be well tolerated and more effective than placebo in the treatment of early-stage PD.1-3
- Objective:
  - To assess the long-term safety, tolerability, and efficacy of rotigotine transdermal system in subjects with idiopathic PD.

Methods
Study Design
- This was an open-label, long-term extension (SP702, clinicaltrials.gov NCT00394145) of the 6-month, double-blind study (Figure 1).
- Subjects completing the double-blind study had the option of long-term treatment with rotigotine in the open-label extension.

Results
Subjects
- 217 of 277 subjects (78%) completed the double-blind study and entered the open-label extension.
- 60 (22%) subjects did not enter the extension; 54 were ineligible due to non-completion of the double-blind study and 6 opted not to participate.
- 47% of subjects remained in the study upon closure by the sponsor; 24% withdrew prematurely due to adverse events and 6% due to lack of efficacy.

Efficacy
- Adverse events.
- Unified Parkinson’s Disease Rating Scale (UPDRS) Part II (activities of daily living) + Part III (motor examination) sum score.

Safety
- There were no clinically relevant changes in vital signs or ECG findings.
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Table 2. Mean change from double-blind baseline in UPDRS (II+III) (full analysis set, LOCF, n=177)

At 2 years of open-label treatment, 57 subjects included in the full analysis set for the double-blind phase were not included in the safety set for the open-label extension. Subjects did not complete the double-blind phase and were not eligible for open-label treatment; an auxiliary cohort who completed the double-blind phase but did not enter the open-label extension, and an auxiliary cohort who did not return to the clinic following enrolment in the open-label extension.

Conclusions
- Rotigotine transdermal system was generally well tolerated by subjects with idiopathic PD for up to 5 years of treatment.
- Mean UPDRS (I + II) scores declined from an initial -5.0 point improvement to the double-blind baseline value in the first 2 years of open-label treatment, and remained within 4 points of the baseline value thereafter.

* Doubled-blind placebo

Figure 3. Mean change from double-blind baseline in UPDRS (II+III)

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