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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

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Background

- The development of motor complications in patients with Parkinson's disease (PD) is associated with pulsatile stimulation of dopamine receptors, especially when using short-acting dopaminergic agents.[1]
- Pulsatile stimulation due to fluctuating plasma levels of orally administered dopamine agonists may limit the long-term effectiveness of these drugs.[1,2]
- 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.[1]
- 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.[1,2]

Objective

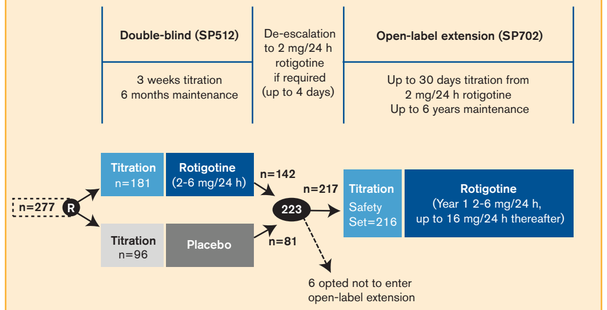
- To assess the long-term safety, tolerability, and efficacy of rotigotine transdermal system in subjects with idiopathic PD.

Methods

Study Design

- This was an open-label, long-term extension (SP702, clinicaltrials.gov:NCT00594165) 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.

Figure 1. SP702 study design



Subject Eligibility

- Double-blind study:
  - Early-stage idiopathic PD (≤5 years duration)
  - Hoehn and Yahr Stage I - III
  - No previous or concurrent therapy with a dopamine agonist, or with carbidopa/levodopa within 28 days of baseline.
- Open-label extension:
  - Completion of the double-blind maintenance period
  - No ongoing serious adverse event related to trial medication
  - Concomitant levodopa permitted, if required, after 1 month of rotigotine maintenance therapy.

Outcome measures

- Extent of exposure to rotigotine.
- Adverse events.
- Unified Parkinson's Disease Rating Scale (UPDRS) Part II (activities of daily living) + Part III (motor examination) sum score.
- Safety and efficacy analyses were performed for the safety set, defined as all subjects who received at least one dose of 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 six 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.

Table 1. Demographic and baseline characteristics (double-blind baseline)

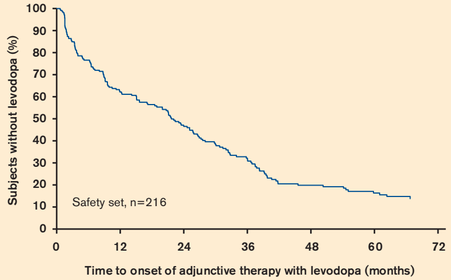
	Safety set* (n=216)
Age, mean ± SD, years	63.2 ± 10.3
Male, n (%)	147 (68.1)
Caucasian, n (%)	209 (96.8)
Mean duration of PD (range), years	1.3 (0-6)
UPDRS Part II Score, mean ± SD	8.1 ± 4.3
UPDRS Part III Score, mean ± SD	21.1 ± 8.3
UPDRS (II + III) Sum Score, mean ± SD	29.2 ± 11.0
Prior or concomitant PD medications, n (%)	97 (44.9)

*One subject received open-label trial medication at the final visit of the double-blind phase, but never returned to the clinic and was therefore excluded from the safety set

Rotigotine Exposure

- 112 (52%) subjects received at least 5 years of rotigotine treatment.
- Mean ± SD rotigotine dose at 5 years was 10.0 ± 3.6 mg/24 h.

Figure 2. Time to onset of adjunctive levodopa therapy



- During open-label treatment (up to 6 years) 57 subjects (26%) remained on rotigotine monotherapy and 159 subjects (73%) started levodopa co-therapy.

Safety

- There were no clinically relevant changes in vital signs or ECG findings.

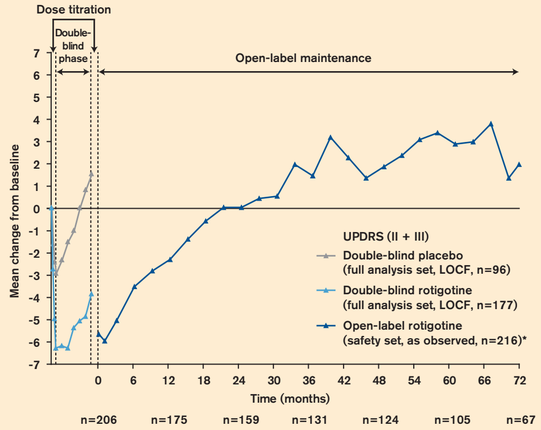
Table 2. Most frequently reported treatment-emergent adverse events during open-label treatment

Adverse event (Reported by ≥10% of subjects)	n (%) (Safety set, n=216)	Exposure-adjusted incidence (% per subject-year)
Somnolence	116 (53.7)	23.4
Fall	71 (32.9)	16.5
Oedema peripheral	80 (37.0)	14.2
Nausea	66 (30.6)	12.4
Application and instillation site reactions*	70 (32.4)	11.7
Arthralgia	51 (23.6)	9.9
Dizziness	58 (26.9)	9.4
Back pain	53 (24.5)	8.3
Pain in extremity	40 (18.5)	7.6
Urinary tract infection	33 (15.3)	6.6
Insomnia	47 (21.8)	6.2
Upper respiratory tract infection	33 (15.3)	5.7
Vomiting	26 (12.0)	5.2
Constipation	37 (17.1)	4.9
Depression	38 (17.6)	4.9
Cataract	25 (11.6)	4.5
Nasopharyngitis	25 (11.6)	3.5
Hallucination	22 (10.2)	3.5
Hypertension	28 (13.0)	3.3
Anxiety	24 (11.1)	3.2
Fatigue	24 (11.1)	2.8

*Higher-level term

Efficacy

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



*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: 50 subjects did not complete the double-blind phase and were not eligible for open-label treatment, six subjects who completed the double-blind phase opted not to enter the open-label extension, and one subject did not return to the clinic following enrolment in the open-label extension

- Mean UPDRS (II + III) scores declined from an initial -5.6 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.

- At End of Maintenance 25% of subjects were classed as UPDRS (II + III) responders, defined as subjects who experienced at least a 20% decrease in UPDRS (II + III) from double-blind baseline.

Conclusions

- Rotigotine transdermal system was generally well tolerated by subjects with idiopathic PD for up to 6 years of treatment.
- Mean UPDRS (II + III) scores demonstrated sustained efficacy of rotigotine over 2 years of open-label treatment.

*Rotigotine transdermal system (Neupro®, UCB Pharma GmbH) is approved for the treatment of early stage idiopathic PD in the US, and early and advanced stage PD, as well as moderate-to-severe idiopathic restless legs syndrome in the EU.

References
1. Watts RL, Jankovic J, Waters C, et al. Randomized, blind, controlled trial of transdermal rotigotine in early Parkinson disease. *Neurology*. 2007;68(4):272-276. **2.** Jankovic J, Watts RL, Martin W, et al. Transdermal rotigotine: double-blind, placebo-controlled trial in Parkinson Disease. *Arch Neurol*. 2007;64(5):676-682. **3.** Jenner P. A novel dopamine agonist for the transdermal treatment of Parkinson's disease. *Neurology*. 2005;65(2 Suppl 1):S3-S5.

Acknowledgements and Disclosures
This study was supported by SCHWARZ BIOSCIENCES, Inc., a member of the UCB Group of Companies. Editorial assistance in the development of this poster was provided by Hannah Carney (Evidence Scientific Solutions) and was contracted by UCB Pharma S.A.
R Watts has received research support and personal compensation for consulting and advisory board services from SCHWARZ BIOSCIENCES. B Boroojerdi is an employee of SCHWARZ BIOSCIENCES GmbH, a member of the UCB Group of Companies, and receives stock options from this employment.
J Jankovic has received personal compensation for consulting services from Allergan, Inc., Biovail, Michael J Fox Foundation for Parkinson Research, Merz Pharmaceuticals, Lundbeck Inc., and Teva Neuroscience; and has received research support from Allergan, Inc., Boehringer Ingelheim, Inc., Ceregene Inc., Chiltern International, Impax Pharmaceuticals, Ipsen Limited, Medtronic, Inc., Merz Pharmaceuticals, St. Jude Medical, and Teva Neuroscience. He has received personal compensation in an editorial capacity for *Medlink: Neurology*.

Presented at the 62nd American Academy of Neurology Annual Meeting, April 10-17, 2010, Toronto, Canada.