Approved by UCB 13-Nov-2008

Clinical Study Summary (CSS)

CT Registry ID#: *NCT00593606 (ClinicalTrials.gov Identifier number)*
Study No.: SP908

These results are supplied for informational purposes only. Prescribing decisions should be made based on the approved package insert.

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Neupro® transdermal patch	Rotigotine	Parkinson's disease

Name of Sponsor/Company: SCHWARZ PHARMA Korea

Title of Study:
A Phase 3b, open-label, multicenter trial to assess the safety and tolerability of switching Korean subjects from ropinirole to the rotigotine transdermal system and its effect on symptoms in idiopathic Parkinson's disease

Investigator(s) (number only): 8

Study Center(s) (number only): 8

Length of Study:	Maximum of approximately 12 weeks per patient	Phase of Development: 3b
Date first patient enrolled:	23 Jul 2007	
Date last patient completed:	28 Dec 2007	

Abstract:

SP908 was an open-label, multicenter trial to assess the safety and tolerability of overnight switching from ropinirole to the rotigotine transdermal system and its effect on symptoms in Korean subjects with idiopathic Parkinson's disease.

Safety was evaluated by extent of exposure, analysis of adverse events (AEs) and clinical laboratory evaluations, physical and neurological examinations, changes in vital signs, body weight, and electrocardiograms (ECGs), assessment of application sites, and results of the Modified Minnesota Impulsive Disorder Interview. Tolerability was assessed by the following: total number of subjects completing the trial, with or without dose adjustments in their original rotigotine dose assignment; total number of subjects who discontinued or had dose reductions during the 5 half-life overlap period (ie, subjects who dropped out during the 5 half-life overlap period due to AEs, subjects who dropped out due to an AE with onset during the 5 half-life overlap period, subjects who required a dose reduction during the 5 half-life overlap period due to an AE, and subjects who required a dose reduction due to an AE with onset during the 5 half-life overlap period); incidence rates of AEs prior to, during, and after the switch (5 half-life overlap period) to rotigotine.

Efficacy of rotigotine was assessed by change from Baseline to the End of Treatment in the Unified Parkinson's Disease Rating Scale (UPDRS) Parts I, II, III, and IV scores; improvements in sleep as measured by the Parkinson's Disease Sleep Scale (PDSS) and the Epworth Sleepiness Scale (ESS); improvement in non-motor symptoms as measured by the Parkinson's Disease Non-motor Symptom Assessment Scale (PDNMS); severity of illness and global improvement as measured by the Clinical Global Impression (CGI), Patient Global Impression (PGI), and Parkinson's Disease Questionnaire

(short form) (PDQ-8); and a patient treatment preference scale.
Blood sampling at the End of Treatment Visit was done to assess the plasma concentration of rotigotine in the target Korean Parkinson's disease population.

Main inclusion criteria included male or female Korean patients, aged ≥18 years, with idiopathic Parkinson's disease (Hoehn and Yahr Stage I to IV) as defined by the cardinal sign, bradykinesia, and at least 1 of the following: resting tremor, rigidity, or impairment of postural reflexes. Subject was not satisfactorily controlled on a total daily dose of ropinirole from 3mg to 12mg, inclusive. If the subject was receiving levodopa, either short-acting or sustained-release (in combination with benserazide or carbidopa), the total daily dose must have been stable for 28 days prior to the Baseline Visit and must have remained stable for the Treatment Period. If the subject was receiving an anticholinergic agent (eg, benztropine, trihexyphenidyl, parsitan, procyclidine, biperiden), a monoamine oxidase B inhibitor (eg, selegiline), a catechol-O-methyltransferase inhibitor (eg, entacapone), or an N-methyl-d-aspartate antagonist (eg, amantadine), he/she must have been on a stable dose for at least 28 days prior to the Baseline Visit and must have been maintained on that dose for the Treatment Period.

At the Baseline Visit, patients were dispensed rotigotine patches at a dose considered equivalent to the dose of ropinirole that the subject was currently taking. Patients on ropinirole 3mg/day were switched to rotigotine 2mg/24h, and those using ropinirole 6mg/day were switched to rotigotine 4mg/24h; patients on ropinirole 8mg/day and 9mg/day were switched to rotigotine 6mg/24h, and those taking ropinirole 12mg/day were switched to rotigotine 8mg/24h.

The trial included a Pretreatment Period (within 28 days before the overnight switch to rotigotine), a Baseline Visit (Day 0), and a 28-day Treatment Period. Subjects completed the End of Treatment assessments, entered a De-escalation Period (up to 6 days), and returned in 28 days for a Safety Follow-Up Visit.

Number of Patients:	
Planned, N:	120
Enrolled, N:	124
Treated, n (%)	116 (93.5)
Completed Treatment Period, n (%):	99 (85.3)
Withdrawn at any time, n (%):	19 (16.4)
Withdrawn due to Adverse Events, n (%):	13 (11.2)
Withdrawn for Other Reasons, n (%):	6 (5.2)
Demography:	
Gender (Females/Males):	47/69
Age (years), mean(SD):	60.0 (10.1)
Race, n (%):	Asian, 116 (100.0)

Safety Outcomes:

Switching from ropinirole to the rotigotine transdermal patch was generally well tolerated. Approximately 89% of subjects completing the Treatment Period did not require a dose adjustment. Adverse events were consistent with the expected effects of dopamine receptor stimulation and the

use of a transdermal delivery system. Subjects reported AEs that were generally mild or moderate in intensity. No subject experienced a serious adverse event (SAE). A total of 13 subjects (11%) reported 19 AEs leading to discontinuation. Three subjects (3%) experienced AEs that led to dose reductions.

Nine subjects (8%) withdrew from the trial and 1 subject (<1%) had a reduction in rotigotine dose due to AEs with onset during the 5 half-life overlap period when switching from ropinirole to rotigotine. No subject withdrew from the trial and 1 subject (<1%) had a reduction in rotigotine dose during the 5 half-life overlap period due to AEs when switching from ropinirole to rotigotine. The AE incidence rate (AEs/day) was highest during the switch between ropinirole and rotigotine (0.112) as compared to prior to (0.004) or after (0.008) the switch.

The most common treatment-emergent AEs (TEAEs) (ie, those having an incidence ≥5%) included dizziness, tremor, dyskinesia, and asthenia. Changes in clinical laboratory values were minimal. No ECG changes were attributable to rotigotine treatment.

Treatment Emergent AEs	**Total (N=116)**
TEAEs with incidence ≥2%, n (%): (preferred term)	
Any AE	45 (38.8)
Dizziness	7 (6.0)
Tremor	7 (6.0)
Dyskinesia	6 (5.2)
Asthenia	6 (5.2)
Muscle rigidity	5 (4.3)
Bradykinesia	4 (3.4)
Somnolence	4 (3.4)
Dry mouth	4 (3.4)
Application and instillation site reactions[a]	3 (2.6)
Application site pruritus	3 (2.6)
a. MedDRA High Level Term	
Drug-related TEAEs (as determined by the investigator):	**Total (N=116)**
Drug-related TEAEs in >2 subjects, n (%): (preferred term)	
All drug-related AEs	32 (27.6)
Tremor	7 (6.0)
Dyskinesia	5 (4.3)
Dizziness	5 (4.3)
Bradykinesia	4 (3.4)
Asthenia	4 (3.4)
Application and instillation site reactions[a]	3 (2.6)
Application site pruritus	3 (2.6)
a. MedDRA High Level Term	

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Death, SAEs, and Other SAEs (if applicable):	
Death, n (%):	0
Patients with SAEs, n(%):	0
Outcomes: This was an open-label exploratory trial. On average, subjects switched from ropinirole to the rotigotine transdermal patch experienced no loss of efficacy. Small improvements were seen in UPDRS Parts I to IV scores. Improvements in Parkinsonian symptoms were seen in subjects upon switching to rotigotine, as assessed by a variety of standard Parkinson's disease scales, including the PDNMS, CGI, PGI, and PDQ-8. There were no substantial changes in the PDSS and ESS. Plasma concentrations of unconjugated and total rotigotine in this trial were comparable to plasma concentrations obtained in prior clinical trials with the rotigotine transdermal patch.	
Publication Reference(s) based on the study: None	
Date of report: 14 Aug 2008	