CT Registry ID#: NCT00243945 (ClinicalTrials.gov Identifier number)
Study No.: SP826

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®	Rotigotine	Idiopathic Parkinson's disease

Name of Sponsor/Company: SCHWARZ BIOSCIENCES, A member of the UCB group

Title of Study:
A phase 3b, open-label, multicenter, multinational trial to evaluate the effects of rotigotine transdermal patch on early morning motor impairment and sleep disorders in patients with idiopathic Parkinson's disease

Investigator(s) (number only): 6

Study Center(s) (number only): 6

Length of Study:	Maximum 22 weeks per patient	Phase of Development: 3b
Date first patient enrolled:	24 Dec 2004	
Date last patient completed:	21 Jul 2005	

Abstract:
SP826 was an open-label, multicenter, multinational trial to evaluate the effects of the rotigotine transdermal patch on early morning motor impairment and sleep disorders in subjects with idiopathic Parkinson's disease. Male or female subjects ages 18 to 85 years with idiopathic Parkinson's disease (Hoehn & Yahr Stage I-IV) with cardinal sign bradykinesia, and at least 1 of the following: resting tremor, rigidity, or impairment of postural reflexes were included. A subject was required to have unsatisfactory control of early morning motor impairment as determined by the investigator. If a subject was taking levodopa with or without Catechol-O-methyl transferase (COMT) inhibitors, he/she must have been on a stable dose of levodopa (in combination with benserazide or carbidopa) with or without COMT inhibitors for at least 28 days prior to Baseline. If the subject was receiving an anticholinergic agent (eg, benztropine, trihexyphenidyl, parsitan, procyclidine, biperiden), a monoamine oxidase B (MAO-B) inhibitor (eg, selegiline), or an n-methyl-d-aspartate (NMDA) 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 duration of the trial.

Each subject was to complete a Screening Phase (within 28 days before the start of trial medication), a Baseline Phase, a Titration Phase (up to 8 weeks), a 4-week Maintenance Phase, and a De-escalation Phase (up to 14 days) (for subjects who selected not to continue into the open-label extension [SP833]). After the De-escalation Phase, subjects returned for a Safety Follow-Up Visit in 30 days.

All subjects commenced the Titration Phase at a daily dose of 2mg/24h for 1 week. Thereafter, the dose was increased at 7-day intervals in 2mg/24h increments until either the optimal dose was identified or the Titration Phase was complete and the maximum daily dose of 16mg/24h was reached. The optimal dose was defined as the dose at which both the investigator and subject felt that early morning motor impairment was adequately controlled. The subject remained at the optimal/maximum dose throughout the 4-week Maintenance Phase. At cessation of therapy, the dose

of rotigotine was reduced gradually (by 2mg/24h every 2 days) over 14 days (depending on maintenance dose level) for those subjects who did not select to enter the open-label extension.

Number of Patients:	
Planned, N:	50
Enrolled/Treated, N:	58/54
Completed, n (%):	48 (89)
Number of Patients Withdrawn, n (%):	6 (11)
Withdrawn due to Adverse Events, n (%):	5 (9)
Withdrawn for Other Reasons, n (%):	1 (2)

Demography:	
Gender (Females/Males):	19/35
Age (years), mean (SD):	65.0 ± 10.0
Duration of PD (Mean ± SD), years:	5.25 ± 3.43
Patients on concomitant levodopa, n (%)	52 (96)

Safety Outcomes:

- **Summary of treatment-emergent adverse events, deaths, other serious adverse events and certain other significant adverse events:**

Thirty-eight subjects (70%) reported an adverse event (AE) during the treatment period. Five patients (5/54 = 9%) discontinued during the trial due to an AE. Adverse events leading to discontinuation included application and instillation site reactions (n=3), nausea (n=1), somnolence (n=1), fatigue (n=1), and pain (n=1). Three subjects reported a total of 4 serious treatment-emergent adverse events (Parkinsonism, back pain, rib fracture, humerus fracture). Each SAE was judged by the investigator to be either not related or unlikely related to trial medication.

Three subjects experienced perception disturbances; moderate visual hallucination (n=1), mild illusion (n=1), and moderate illusion (n=1). Seven subjects developed treatment-emergent asymptomatic orthostatic hypotension (OH), and 15 subjects that met the criteria for OH at the Screening Visit or Baseline also had asymptomatic OH at 1 or more evaluations during treatment. Eleven (20%) subjects reported at least 1 application and instillation site reaction, including application site pruritus, reaction, dermatitis, erythema, pain, and irritation. These AEs were usually well tolerated and mild or moderate in intensity, with the exception of 1 severe application site reaction. None of the application and instillation site reactions were reported as an SAE. No sleep attacks were reported in this trial. There were no clinically relevant changes in vital signs, laboratory parameters (including ECG), neurological or physical signs.

Treatment Emergent AEs (TEAE):
TEAEs occurring in ≥5% of patients:

System Organ Class / Preferred Term	N=54 *n (%)*
Any AE	38 (70)
Nervous system disorders	18 (33)
Somnolence	6 (11)
Dizziness	3 (6)

Dyskinesia	3 (6)
Headache	3 (6)
General disorders and administration site conditions	14 (26)
Application and instillation site reactions[a]	11 (20)
Application site pruritus	5 (9)
Application site reaction	4 (7)
Gastrointestinal disorders	13 (24)
Nausea	11 (20)
Psychiatric disorders	10 (19)
Disturbances in initiating and maintaining sleep[a]	6 (11)
Insomnia	5 (9)
Perception disturbances[a]	3 (6)
Injury, poisoning, and procedural complications	5 (9)
Fall	4 (7)
Skin and subcutaneous tissue disorders	5 (9)
Dermatitis contact	4 (7)
Infections and infestations	3 (6)
Influenza	3 (6)
Investigations	3 (6)

a. This is a MedDRA High Level Term and was used as the 5% cutoff for these AEs.

Drug-related TEAEs (as assessed by the Investigator) :

Drug-related TEAEs occurring in ≥5% of patients:

System Organ Class / Preferred Term	N=54 n (%)
Any AE	31 (57)
Nervous system disorders	13 (24)
Somnolence	4 (7)
Dizziness	3 (6)
General disorders and administration site conditions	13 (24)
Application and instillation site reactions[a]	11 (20)
Application site pruritus	5 (9)
Application site reaction	4 (7)
Gastrointestinal disorders	8 (15)
Nausea	8 (15)
Psychiatric disorders	9 (17)
Disturbances in initiating and maintaining sleep[a]	5 (9)
Insomnia	4 (7)
Perception disturbances[a]	3 (6)
Skin and subcutaneous tissue disorders	4 (7)
Contact dermatitis	4 (7)

a. This is a MedDRA High Level Term and was used as the 5% cutoff for these AEs.

Death, SAEs, and Other SAEs:

CT Registry ID#: NCT00243945 (ClinicalTrials.gov Identifier number) **Study No.: SP826**	
Death, n (%):	0
Patients with treatment-emergent SAEs, n (%):	3 (6)
System Organ Class / Preferred Term	*n (%) [n considered drug-related by the Investigator]*
Injury, Poisoning and Procedural Complications	2 (4) [0]
Rib fracture	1 (2) [0]
Humerus fracture	1 (2) [0]
Musculoskeletal and connective tissue disorders	1 (2) [0]
Back pain	1 (2) [0]
Nervous system disorders	1 (2) [0]
Parkinsonism	1 (2) [0]

Primary & Secondary Outcomes:
This was an open-label exploratory trial with no specified primary or secondary efficacy endpoints.

Subjects experienced improved control of motor performance as supported by improvements in UPDRS Part III Score, with a mean change from Baseline to end of Maintenance of -9.3 (Full Analysis Set) and -11.5 (Per Protocol Set). The mean changes between average evening Tapping Rates, average morning Tapping Rates, and the difference between morning and evening average Tapping Rates at the End of Maintenance compared to Baseline for the average of both sides and the dominant affected side showed improvement in motor performance. The mean Nocturnal Akinesia Score decreased from Baseline to the End of Maintenance, indicating improvement of evening motor performance, and a mean decrease in the Standing-Walking-Turning time indicates improvement of morning motor performance.

Subjects experienced improved control of sleep-related disorders as supported by decreased nocturnal akinesia (Nocturnal Akinesia Score, NADCS Sum Score), decreased nocturnal dystonia (Nocturnal Dystonia Score, NADCS Sum Score), decreased nocturnal cramps (Nocturnal Cramps Score, NADCS Sum Score), fewer nocturias, and improved sleep and nocturnal disability (PDSS Sum Score). Subjects also experienced improved sleep without daytime somnolence as supported by a decrease in the ESS Score.

Publication Reference(s) based on the study:
None at this time

Date of report: 04-May-2006