

Clinical Study Summary (CSS)

These results are sumplied for infe	ormational purposes only	Prescrib	hing decisions should	d he made based on the	
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Proprietary Drug Name	INN		Therapeutic area		
Neupro [®] transdermal patch	Rotigotine		Restless legs syndr		
Name of Sponsor/Company: SC	CHWARZ BIOSCIENC	ES, Gmb	H, A member of th	e UCB group	
Title of Study:		. 1	11.1	1	
A multicenter, double-blind, rand investigate the efficacy and safety					
	11	e in subje	ets with idiopathic re	estiess legs syndrome	
Investigator(s) (number only): Study Center(s) (number only):					
Length of Study:	16 week maximum	Dhase	of Development:	3	
Date first subject enrolled:	24 Nov 2005	1 mase	of Development.	5	
Date last subject completed:	21 Jul 2006				
Abstract:					
SP794 was a Phase 3, multicenter	double-blind randomiz	ed place	o-controlled 2-arm	narallel-group trial in	
subjects with idiopathic restless le					
diagnosis of idiopathic RLS based					
Legs Syndrome Study Group. In a					
for RLS) or have had initial respo	-			-	
International Restless Legs Scale					
score of ≥ 4 points on the Clinical					
	Olouar impressions (CO			ng moderately (11) at	
Daschine, and (+) have a 1 Livit (D'					
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as assessed by the investigator. M	eriodic limb movements/ lain exclusion criteria inc	total time	in bed) of ≥ 15 based	d on polysomnography	
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CT Registry ID#: NCT00275236 (ClinicalTrials.gov Identifier number) Study No. + SP704

Study No.: SP794

and entered the 4-week Maintenance Period. Subjects who completed the 4-week Maintenance Period and a 7-day Taper Period were eligible to participate in an open-label extension trial. Subjects who did not complete the 4-week Maintenance Period or who chose not to participate in the open-label extension trial completed a 30-day Safety Follow-Up Period.

Number of Subjects:	Placebo	Rotigotine	Total
Planned, N:	20	40	60
Enrolled/Randomized, N:	21	46	67
Completed, n (%):	20 (95.2)	41 (89.1)	61 (91.0)
Number of Subjects Withdrawn, n (%):	1 (4.8)	5 (10.9)	6 (9.0)
Withdrawn due to Adverse Events, n (%):	1 (100.0)	2 (40.0)	3 (50.0)
Withdrawn for Other Reasons, n (%):	0	3 (60.0)	3 (50.0)
Demography:			
Gender (Females/Males):	14/7	35/11	49/18
Age (years), mean (SD):	55.2 (10.6)	60.8 (9.4)	59.1 (10.1)
Race, n (%):			
White	21 (100)	46 (100)	67 (100)

Safety Outcomes:

Rotigotine was well tolerated in this trial. Most AEs were consistent with stimulations of dopamine receptors and use of a transdermal patch. The most frequently occurring AEs were nausea, headache, and application site reactions. All application site reactions were mild or moderate in severity and none led to discontinuation from the trial. There was one treatment-emergent serious adverse event (SAE) during the trial which occurred during the Safety-Follow-up Period. Overall, 2 rotigotine-treated subjects and 1 placebo-treated subject discontinued from the trial because of an AE. Overall, there is no evidence for an association between rotigotine treatment and ECG abnormalities or changes at doses up to 6.75mg/day. No clinically relevant changes in vital signs (including orthostatic assessment), clinical chemistry, hematology, endocrine parameters, or urinalysis, physical or neurological examination, or menstrual or sexual function were observed.

A summary of AEs is provided below:				
Treatment Emergent AEs (TEAE):	Placebo (N=21)	Rotigotine total (N=46)		
Subjects with ≥5% TEAEs, n (%): (by Preferred term)				
Any system organ class	12 (57.1)	34 (73.9)		
Nausea	1 (4.8)	10 (21.7)		
Headache	4 (19.0)	9 (19.6)		
Application and instillation site reactions	1 (4.8)	8 (17.4)		
Somnolence	2 (9.5)	6 (13.0)		
Fatigue	2 (9.5)	4 (8.7)		
Constipation	0	3 (6.5)		
Nasopharyngitis	0	3 (6.5)		
Dizziness	0	3 (6.5)		
Insomnia	0	3 (6.5)		



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by the investigator), n (%) (by Preferred term):(N=21)Any system organ class9 (42.9)Nausea1 (4.8)Constipation0Application and instillation site reactions ^a 1 (4.8)Fatigue2 (9.5)Headache3 (14.3)Somnolence2 (9.5)Dizziness0Insomnia0a. High Level Term0Death, SAEs, and Other SAEs:PlaceboDeath, n (%):0Subjects with SAEs, n (%):0Subjects with SAEs0Subjects with SAEs0Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 fcefficacy variable (re	Drug-related TEAEs in ≥5% of Subjects (as determined	Placebo	Rotigotine total
Nausea1 (4.8)Constipation0Application and instillation site reactions ^a 1 (4.8)Fatigue2 (9.5)Headache3 (14.3)Somnolence2 (9.5)Dizziness0Insomnia0a. High Level Term0Death, SAEs, and Other SAEs:PlaceboDeath, n (%):0Subjects with SAEs, n (%):0Subjects with SAEs0Subjects with SAEs0Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 fcefficacy variable (reduction from Baseline in the PLMI at the end of the Maintenance Perithe IRLS sum score (secondary variable) are consistent with the primary analysis. Twenty of rotigotine-treated subjects had a score of 0, reflecting they did not have any RLS sympt the Maintenance Period. The majority of rotigotine-treated subjects (73%)		(N=21)	(N=46)
Constipation 0 Application and instillation site reactions ^a 1 (4.8) Fatigue 2 (9.5) Headache 3 (14.3) Somnolence 2 (9.5) Dizziness 0 Insomnia 0 a. High Level Term 0 Death, SAEs, and Other SAEs: Placebo Death, n (%): 0 Subjects with SAEs, n (%): 0 Subjects with SAEs 0 Subjects with SAEs 0 Verify System Organ Class) 0 Osteoarthritis 0 ^a Event occurred during Safety Follow-up Period 0 Primary & Secondary Efficacy Outcomes: Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 for efficacy variable (reduction from Baseline in the PLMI at the end of the Maintenance Perithe IRLS sum score (secondary variable) are consistent with the primary analysis. Twenty of rotigotine-treated subjects had a score of 0, reflecting they did not have any RLS sympting the Maintenance Period. The majority of rotigotine-treated subjects (73%) achieved a clin of ≤2 on the PLMASI (arousal index) compared to 25% of placebo-treated subjects. Over results in this trial were positive with respect to the objective measures (eg, PLMI); non-P	Any system organ class	9 (42.9)	29 (63.0)
Application and instillation site reactions ^a 1 (4.8)Fatigue2 (9.5)Headache3 (14.3)Somnolence2 (9.5)Dizziness0Insomnia0a. High Level Term0Death, SAEs, and Other SAEs:PlaceboDeath, SAEs, and Other SAEs:0Subjects with SAEs, n (%):0Subjects with SAEs0Subjects with SAEs0Subjects with SAEs0Subjects with SAEs0Subjects with SAEs0Subjects with SAEs0Subjects with SAEs0Osteoarthritis0 ^a Event occurred during Safety Follow-up PeriodPrimary & Secondary Efficacy Outcomes:Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 fcefficacy variable (reduction from Baseline in the PLMI at the end of the Maintenance Perithe IRLS sum score (secondary variable) are consistent with the primary analysis. Twenty of rotigotine-treated subjects had a score of 0, reflecting they did not have any RLS sympting the Maintenance Period. The majority of rotigotine-treated subjects (73%) achieved a clin of ≤2 on the PLMASI (arousal index) compared to 25% of placebo-treated subjects. Over results in this trial were positive with respect to the objective measures (eg, PLMI); non-P	Nausea	1 (4.8)	10 (21.7)
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a. High Level Term Image: constraint of the second arrow of	Dizziness	0	3 (6.5)
Death, SAEs, and Other SAEs:PlaceboDeath, n (%):0Subjects with SAEs, n (%):0Subjects with SAEs0Subjects with SAEs0(by Primary System Organ Class)0Osteoarthritis0a Event occurred during Safety Follow-up PeriodPrimary & Secondary Efficacy Outcomes:Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 fcefficacy variable (reduction from Baseline in the PLMI at the end of the Maintenance Perithe IRLS sum score (secondary variable) are consistent with the primary analysis. Twenty of rotigotine-treated subjects had a score of 0, reflecting they did not have any RLS sympthe Maintenance Period. The majority of rotigotine-treated subjects (73%) achieved a clin of \leq 2 on the PLMASI (arousal index) compared to 25% of placebo-treated subjects. Over results in this trial were positive with respect to the objective measures (eg, PLMI); non-P	Insomnia	0	3 (6.5)
Death, n (%): 0 Subjects with SAEs, n (%): 0 Subjects with SAEs 0 (by Primary System Organ Class) 0 Osteoarthritis 0 ^a Event occurred during Safety Follow-up Period 0 Primary & Secondary Efficacy Outcomes: Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 fc efficacy variable (reduction from Baseline in the PLMI at the end of the Maintenance Perithe IRLS sum score (secondary variable) are consistent with the primary analysis. Twenty of rotigotine-treated subjects had a score of 0, reflecting they did not have any RLS symptime Maintenance Period. The majority of rotigotine-treated subjects (73%) achieved a clini of ≤2 on the PLMASI (arousal index) compared to 25% of placebo-treated subjects. Over results in this trial were positive with respect to the objective measures (eg, PLMI); non-P	a. High Level Term		
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Osteoarthritis 0 a Event occurred during Safety Follow-up Period 0 Primary & Secondary Efficacy Outcomes: 0 Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 for efficacy variable (reduction from Baseline in the PLMI at the end of the Maintenance Periot the IRLS sum score (secondary variable) are consistent with the primary analysis. Twenty of rotigotine-treated subjects had a score of 0, reflecting they did not have any RLS sympthe Maintenance Period. The majority of rotigotine-treated subjects (73%) achieved a clim of ≤2 on the PLMASI (arousal index) compared to 25% of placebo-treated subjects. Over results in this trial were positive with respect to the objective measures (eg, PLMI); non-P	Subjects with SAEs		
^a Event occurred during Safety Follow-up Period Primary & Secondary Efficacy Outcomes: Superiority of rotigotine over placebo was demonstrated at a significance level of 0.025 for efficacy variable (reduction from Baseline in the PLMI at the end of the Maintenance Peri- the IRLS sum score (secondary variable) are consistent with the primary analysis. Twenty of rotigotine-treated subjects had a score of 0, reflecting they did not have any RLS sympt the Maintenance Period. The majority of rotigotine-treated subjects (73%) achieved a clim of ≤ 2 on the PLMASI (arousal index) compared to 25% of placebo-treated subjects. Over results in this trial were positive with respect to the objective measures (eg, PLMI); non-P	(by Primary System Organ Class)		
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results in this trial were positive with respect to the objective measures (eg, PLMI); non-P	the IRLS sum score (secondary variable) are consistent with th	iu not nave any KLS	
	the IRLS sum score (secondary variable) are consistent with th of rotigotine-treated subjects had a score of 0, reflecting they d the Maintenance Period. The majority of rotigotine-treated sub-	jects (73%) achieved	
related to sleep (ie, non-movement secondary efficacy parameters) did not show pronound	the IRLS sum score (secondary variable) are consistent with th of rotigotine-treated subjects had a score of 0, reflecting they d the Maintenance Period. The majority of rotigotine-treated sub of \leq 2 on the PLMASI (arousal index) compared to 25% of place	jects (73%) achieved cebo-treated subjects	. Overall, the efficacy
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Date of report: 05-Dec-2008