Study No.: 101468/248

Title: An Open-Label Extension Study with REQUIP™ (ropinirole) CR [Ropinirole XL] for Subjects from Studies 101468/165, 101468/168 and 101468/169

Rationale: Study 101468/248 was conducted to evaluate the safety profile of ropinirole extended release in subjects with early and advanced Parkinson's disease.

Phase: III

Study Period: 13Feb2004 - 31Mar2010

Study Design: Open-label, flexible dose extension of studies 101468/165 (165) 101468/168 (168) and 101468/169 (169)

Centres: Forty-two centers in nine countries: Europe (Belgium, Czech Republic, France, Hungary, Italy, Poland, Spain and the United Kingdom), and 25 centers were in the United States of America (USA)

Indication: Parkinson's disease

Treatment: Ropinirole extended release

Objectives: The primary objective of this study was to evaluate the safety profile of ropinirole extended release tablets during long-term treatment in subjects with early and advanced Parkinson's disease

Primary Outcome/Efficacy Variable: None

Secondary Outcome/Efficacy Variable(s): None

Statistical Methods: None

Study Population: Men and women with early or late phase Parkinson's disease, who had completed studies 165 (pharmacokinetic dose proportionality study) or 168 (uncontrolled monotherapy study in early Phase Parkinson's disease) or subjects who had completed at least 12 weeks of randomized treatment in study 169 (adjunctive therapy study in late Phase Parkinson's disease)

	Ropinirole XL	
Number of Subjects:	419	
Planned, N	N/A	
Entered, N	419	
Completed, n (%)	151 (36)	
Total Number Subjects Withdrawn, N (%)	268 (64)	
Withdrawn due to Adverse Events n (%)	104 (25)	
Withdrawn due to Lack of Efficacy n (%)	5 (1)	
Withdrawn for other reasons n (%)	159 (38)	
Demographics		
N (ITT)	N/A	
Females: Males	160:259	
Mean Age, years (SD)	64.3 (9.81)	
White/Caucasian, n (%)	409 (98)	

Primary Efficacy Results: N/A

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	Ropinirole XL	
Mean Baseline (SE)	N/A	
Difference between treatments (as appropriate to endpoint)	N/A	
95% Confidence Interval		
p-value		

Secondary Outcome Variable(s):		
	Ropinirole XL	
Secondary endpoint	N/A	
Difference between treatments (as appropriate to endpoint)	N/A	
95% CI (if appropriate)	N/A	
An on therapy adverse event (AE) was defined as an AE with onset on or after the start date of study medication but not later than the last date of study medication. An on therapy serious adverse event (SAE) was defined as a SAE with onset on or after the start date of study medication and but not later than the last date of study medication.		
	Ropinirole XL	
N (Safety)	**419**	
Most Frequent Adverse Events – On-Therapy	**n (%)**	
Most Frequent Adverse Events – On-Therapy (5 most frequently reported)		
Subjects with any AE(s), n(%)	365 (87)	
Back pain	58 (14)	
Hallucination	54 (13)	
Peripheral Edema (Oedema Peripheral)	48 (11)	
Somnolence	47 (11)	
Dyskinesia	35 (8)	
Serious Adverse Events - On-Therapy **n (%) [n considered by the investigator to be related to study medication]**		
	Ropinirole XL	
N (Safety)	**419**	
Subjects with non-fatal SAEs, n (%)	95 (23)	
	n (%) [related]	
Parkinson's disease	10 (2) [0]	
Pneumonia	7 (2) [0]	
Angina pectoris	5 (1) [1]	
Coronary artery disease	4 (<1) [0]	
Back pain	4 (<1) [0]	
Dyskinesia	3 (<1) [3]	
Fall	3 (<1) [0]	
Osteoarthritis	3 (<1) [0]	
Psychotic disorder	3 (<1) [3]	
Urinary retention	3 (<1) [0]	
Sciatica	2 (<1) [0]	
Gastroenteritis	2 (<1) [0]	
Urinary tract infection	2 (<1) [0]	
Femoral neck fracture	2 (<1) [0]	
Humerus fracture	2 (<1) [0]	
Non-cardiac chest pain	2 (<1) [0]	
Hallucination	2 (<1) [1]	
Inguinal hernia	2 (<1) [0]	
Hypertensive crisis	2 (<1) [0]	
Cholelithiasis	2 (<1) [0]	
Hyponatraemia	2 (<1) [0]	
Benign prostatic hyperplasia	2 (<1) [0]	
Arrhythmia	2 (<1) [0]	
Akinesia	1 (<1) [0]	

Balance disorder	1 (<1) [0]	
Cerebral haemorrhage	1 (<1) [0]	
Cerebrovascular spasm	1 (<1) [0]	
Hypokinesia	1 (<1) [0]	
Neuroleptic malignant syndrome	1 (<1) [0]	
Radicular syndrome	1 (<1) [0]	
Syncope	1 (<1) [0]	
Acute tonsillitis	1 (<1) [0]	
Appendicitis	1 (<1) [0]	
Bronchitis	1 (<1) [0]	
Device related infection	1 (<1) [0]	
Diverticulitis	1 (<1) [0]	
Erysipelas	1 (<1) [0]	
Localised infection	1 (<1) [0]	
Necrotising fasciitis	1 (<1) [0]	
Pneumonia streptococcal	1 (<1) [0]	
Staphylococcal infection	1 (<1) [0]	
Contusion	1 (<1) [0]	
Femur fracture	1 (<1) [0]	
Forearm fracture	1 (<1) [0]	
Hand fracture	1 (<1) [0]	
Hip fracture	1 (<1) [0]	
Limb injury	1 (<1) [0]	
Post procedural complication	1 (<1) [0]	
Post-traumatic pain	1 (<1) [0]	
Rib fracture	1 (<1) [0]	
Spinal compression fracture	1 (<1) [0]	
Splenic injury	1 (<1) [0]	
Upper limb fracture	1 (<1) [0]	
Vascular pseudoaneurysm	1 (<1) [0]	
Wound	1 (<1) [0]	
Atrial flutter	1 (<1) [0]	
Bradycardia	1 (<1) [0]	
Mitral valve incompetence	1 (<1) [0]	
Ventricular arrhythmia	1 (<1) [0]	
Chest pain	1 (<1) [0]	
Device breakage	1 (<1) [0]	
Device dislocation	1 (<1) [0]	
Gait disturbance	1 (<1) [0]	
Malaise	1 (<1) [0]	
Costochondritis	1 (<1) [0]	
Intervertebral disc disorder	1 (<1) [0]	
Intervertebral disc protrusion	1 (<1) [0]	
Mobility decreased	1 (<1) [0]	
Musculoskeletal chest pain	1 (<1) [0]	
Scoliosis	1 (<1) [0]	
Spinal column stenosis	1 (<1) [0]	
Spinal osteoarthritis	1 (<1) [0]	
Anxiety	1 (<1) [1]	
Confusional state	1 (<1) [0]	
Delirium	1 (<1) [1]	
Depression	1 (<1) [0]	
Hallucination, auditory	1 (<1) [1]	
Hallucination, visual	1 (<1) [1]	
Hallucinations, mixed	1 (<1) [1]	

Paranoia	1 (<1) [1]	
Abdominal pain	1 (<1) [0]	
Aphthous stomatitis	1 (<1) [0]	
Diarrhoea	1 (<1) [0]	
Duodenal ulcer	1 (<1) [0]	
Gastric ulcer perforation	1 (<1) [0]	
Gastrointestinal inflammation	1 (<1) [1]	
Ileus	1 (<1) [0]	
Peritonitis	1 (<1) [0]	
Breast cancer in situ	1 (<1) [0]	
Malignant melanoma	1 (<1) [1]	
Metastases to central nervous system	1 (<1) [0]	
Non-small cell lung cancer	1 (<1) [0]	
Ovarian cancer	1 (<1) [0]	
Prostate cancer	1 (<1) [0]	
Thyroid cancer	1 (<1) [0]	
Uterine cancer	1 (<1) [0]	
Aortic aneurysm	1 (<1) [0]	
Deep vein thrombosis	1 (<1) [0]	
Hypertension	1 (<1) [0]	
Hypotension	1 (<1) [0]	
Lymphoedema	1 (<1) [1]	
Thrombophlebitis	1 (<1) [0]	
Dyspnoea	1 (<1) [0]	
Pneumothorax	1 (<1) [0]	
Respiratory failure	1 (<1) [0]	
Bladder neck obstruction	1 (<1) [0]	
Calculus bladder	1 (<1) [0]	
Cystitis noninfective	1 (<1) [0]	
Haematuria	1 (<1) [0]	
Renal failure chronic	1 (<1) [0]	
Bile duct stone	1 (<1) [0]	
Dehydration	1 (<1) [0]	
Hypokalaemia	1 (<1) [0]	
Ovarian cyst	1 (<1) [0]	
Blood pressure increased	1 (<1) [0]	
Dermatitis contact	1 (<1) [0]	
	Ropinirole XL	
N (Safety)	**419**	
Subjects with fatal SAEs, n (%)	18 (4)	
	n (%) [related]	
Parkinson's disease	2 (<1) [0]	
Death	2 (<1) [0]	
Sudden death	2 (<1) [0]	
Pneumonia aspiration	2 (<1) [0]	
Dementia	1 (<1) [0]	
Multi-organ failure	1 (<1) [0]	
Arrhythmia	1 (<1) [0]	
Atrial fibrillation	1 (<1) [0]	
Cardiovascular insufficiency	1 (<1) [0]	
Myocardial infarction	1 (<1) [0]	
Bronchopneumonia	1 (<1) [0]	
Staphylococcal sepsis	1 (<1) [0]	
Viral infection	1 (<1) [0]	

Acute respiratory failure	1 (<1) [0]	
Colon cancer	1 (<1) [0]	
Lung neoplasm malignant	1 (<1) [0]	
Aortic aneurysm rupture	1 (<1) [0]	

Conclusion:
Within 1 year after study completion this section will either refer you to a publication or contain text interpreting the trial results.