Protocol Registration Receipt
04/24/2014

Long-term Study Of Ropinirole In Restless Legs Syndrome

This study has been completed.

Sponsor:	GlaxoSmithKline
Collaborators:	
Information provided by (Responsible Party):	GlaxoSmithKline
ClinicalTrials.gov Identifier:	NCT00329602

Purpose

This is an initial placebo-controlled study followed by open treatment evaluating the effectiveness and tolerability of ropinirole long-term in patients with moderate to severe Restless Legs Syndrome.

Condition	Intervention	Phase
Restless Legs Syndrome	Drug: Placebo Drug: Ropinirole	Phase 4

Study Type: Interventional

Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study

Official Title: A Parallel Group Study to Evaluate the Efficacy and Safety of Ropinirole for 26 Weeks and to Further Evaluate the Incidence of Augmentation and Rebound for a Further 40 Weeks Open-label Extension Treatment Period in Subjects Suffering From Moderate to Severe Restless Legs Syndrome.

Further study details as provided by GlaxoSmithKline:

Primary Outcome Measure:

- Mean Change From Baseline in the International Restless Legs Syndrome (IRLS) Rating Scale Total Score at Week 12 and Week 26 [Time Frame: Baseline and Weeks 12 and 26] [Designated as safety issue: No]

  A 10-item, participant-reported scale covering different symptoms of the condition. Each item is scored from 0 to 4; 0 represents the absence of a problem and 4 reflects a very severe problem. The best and worst possible scores are 0 and 40, respectively; higher scores represent a greater severity of symptoms. A negative change from baseline indicates improvement, and a negative treatment difference indicates a benefit of Ropinirole IR over placebo. The primary assessment was made by calculating the difference in the average score obtained at Baseline with scores at Week 12 and then Week 26.
- Number of Participants With Clinically Meaningful Augmentation and Early Morning Rebound (EMR) Cases [Time Frame: During 15-month study duration at scheduled (Weeks 16, 20, 26, or early withdrawal for DB phase; Weeks 39, 47, 55, 63, 67, or early withdrawal for the OL phase) and unscheduled (26-week DB phase and 40-week OL phase) visits] [Designated as safety issue: Yes]

  Clinically meaningful augmentation and early morning rebound (EMR) were assessed and confirmed by an independent Adjudication Board. EMR describes the development of RLS symptoms during the early morning, following therapeutic intervention. EMR is differentiated from augmentation, in which the earlier onset of symptoms occurs in the evening.

Secondary Outcome Measures:

- Mean Change From Baseline in the International RLS (IRLS) Rating Scale Total Score at Weeks 1, 4, 8, 16, and 20 [Time Frame: Baseline and Weeks 1, 4, 8, 16, and 20] [Designated as safety issue: No]

  A 10-item, participant-reported scale covering different RLS symptoms. Each item is scored from 0 to 4; 0 represents the absence of a problem and 4 reflects a very severe problem. The best and worst possible scores are 0 and 40, respectively; higher scores represent a greater severity of symptoms. The primary assessment from this study was made by calculating the difference in the average score obtained at Baseline with scores at Weeks 1, 4, 8, 16, and 20. Scores were adjusted for baseline IRLS total score, treatment group, visit, visit by treatment group interaction, and center group.
- Change From Baseline in the Domains of the 12-item Medical Outcomes Study (MOS-12) Sleep Scale at Weeks 12 and 26 [Time Frame: Baseline and Weeks 12 and 26] [Designated as safety issue: No]

  The MOS-12 Sleep Scale is a comprehensive battery, which measures specific aspects of sleep in participants that may have varying co-morbidities, and, as a result, is appropriate for a medically diverse participant population. Domain values are presented on a 0-100 scale, where a higher score means a greater degree of the attribute implied by the scale name. Scores were adjusted for baseline MOS sleep scale domain value, treatment group, visit, visit by treatment interaction, and center group.
- Change From Baseline in Sleep Quantity, a Domain of the 12-item Medical Outcomes Study (MOS-12) Sleep Scale, at Weeks 12 and 26 [Time Frame:

Baseline and Weeks 12 and 26] [Designated as safety issue: No]

The MOS-12 Sleep Scale is a comprehensive battery, which measures specific aspects of sleep in participants that may have varying co-morbidities, and, as a result, is appropriate for a medically diverse participant population.Scores were adjusted for baseline MOS sleep scale domain value, treatment group, visit, visit by treatment interaction, and center group.

- Change From Baseline in the Johns Hopkins RLS Quality of Life (RLS QoL) Questionnaire Overall Life Impact Score at Weeks 12 and 26 [Time Frame: Baseline and Weeks 12 and 26] [Designated as safety issue: No]

  The Johns Hopkins RLS QoL Questionnaire is a disease-specific instrument that assesses the impact of RLS on the daily life, emotional well-being, social life, and work life of participants. The overall life impact score for the John Hopkins RLS QoL scale ranges from a lowest possible score of 0 to a highest possible score of 100. Higher scores represent better quality of life. Scores were adjusted for baseline RLS Quality of Life score, treatment group, visit, visit by treatment interaction, and center group.
- Change From Baseline in the Domains of the MOS 36-item Short Form Health Survey (SF-36) at Weeks 12 and 26 [Time Frame: Baseline and Weeks 12 and 26] [Designated as safety issue: No]

  The MOS SF-36 is a generic QoL instrument measuring functional status and well-being. Positive change from baseline for all domains indicates improvement. For all MOS SF-36 domains, the minimum and maximum scores are 0 and 100, respectively, for the transformed scale. Scores were adjusted for baseline domain score, treatment group, visit, visit by treatment interaction, and center group.
- Percentage of Participants With a Score of Much/Very Much Improved on the Clinical Global Impression-Global Improvement (CGI-I) Scale at Weeks 1, 12 and 26 [Time Frame: Weeks 1, 12 and 26] [Designated as safety issue: No]

  The CGI-I is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-I allows the investigator to rate the participant's global improvement or worsening compared with the condition at Baseline (Day 0). The scale is rated from 1-7 (1 = very much improved; 7 = very much worse). Typically, a participant with a score of 1 or 2 (much improved) is considered a responder.
- Number of Participants Withdrawing Due to Lack of Efficacy During the First 26 Weeks of the Study [Time Frame: Baseline to Week 26] [Designated as safety issue: No]

  Lack of efficacy is defined as up to a 10% improvement in the IRLS Rating Scale total score from the participant's Baseline value and at least 12 weeks of treatment during the double-blind phase.
- Number of Participants Rated as Normal or Borderline Ill on the CGI Severity of Illness (CGI-S) Scale at Week 26 [Time Frame: Week 26] [Designated as safety issue: No]

  The CGI-S scale is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-S allows the investigator to rate the severity of the participant's illness considering their total clinical experience with the subject population being studied and on all information available at the time of rating. The scale is rated from 1-7 (1 = normal, not at all ill; 2 = borderline ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severly ill; 7 = among the most extremely ill participants).
- Median Time to First CGI-I Response of Much/Very Much Improved During the Double-blind Phase [Time Frame: Baseline to Week 26] [Designated as safety issue: No]

  The median time to first CGI-I response of much/very much improved was calculated. The CGI-I is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-I allows the investigator to rate the participant's global improvement or worsening compared with the condition at Baseline (Day 0). The scale is rated from 1-7 (1 = very much improved; 7 = very much worse). Typically, a participant with a score of

1 or 2 (much improved) is considered a responder.

- Number of Participants With a Score of Much/Very Much Improved on the CGI-I Scale at Week 67 [Time Frame: Week 67] [Designated as safety issue: No]

  The CGI-I is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-I allows the investigator to rate the participant's global improvement or worsening compared with the condition at Baseline (Day 0). The scale is rated from 1-7 (1 = very much improved; 7 = very much worse). Typically, a participant with a score of 1 or 2 (much improved) is considered a responder.

- Mean Change From Baseline in the IRLS Rating Scale Total Score at Week 67 [Time Frame: Baseline and Week 67] [Designated as safety issue: No]

  A 10-item, participant-reported scale covering different symptoms of the condition. Each item is scored from 0 to 4, with 0 representing the absence of a problem and 4 reflecting a very severe problem. The best and worst possible scores are 0 and 40, respectively. The primary assessment was made by calculating the difference in the average score obtained at Baseline with score at Week 67.

Enrollment: 404
Study Start Date: March 2006
Study Completion Date: September 2008
Primary Completion Date: September 2008

Arms	Assigned Interventions
Placebo Comparator: Double-blind for 12 to 26 Weeks Double-blind (Ropinirole:Placebo) for 12 to 26 weeks	Drug: Placebo Matching Placebo Drug: Ropinirole Ropinirole IR 0.25mg/day to 4mg/day for RLS
Open-label ropinirole for 40-Weeks Open label ropinirole for 40 weeks	Drug: Ropinirole Ropinirole IR 0.25mg/day to 4mg/day for RLS

A randomised, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of ropinirole for 26 weeks and to further evaluate the incidence of augmentation and rebound for a further 40 weeks open-label extension treatment period in subjects suffering from moderate to severe Restless Legs Syndrome.

Eligibility

Ages Eligible for Study: 18 Years to 79 Years

Genders Eligible for Study: Both

Inclusion Criteria:

- Male and female subjects, between the ages of 18 and 79, inclusive

A female is eligible to enter and participate in the study if she is of:

a. Non-childbearing potential (i.e., physiologically incapable of becoming pregnant, including any female who is post-menopausal); or,
b. Childbearing potential, has a negative result on all required pregnancy tests prior to randomisation, and agrees to an acceptable contraceptive method.

- Subjects with a diagnosis of idiopathic RLS using the RLS Diagnostic Clinical Interview and the International RLS Study Group (IRLSSG) Diagnostic Criteria during the Screening Visit.
- Subjects have had RLS symptoms with a history of a minimum of 15 RLS episodes during the previous month. If this is not possible due to the subject being on previous medication to treat RLS the investigator should ensure that the subject should have experienced 4-5 episodes of RLS symptoms during the last 7 days of the wash-out phase (see below). The subject must discontinue and wash-out any previous medication for the treatment of RLS or sleep prior to the Baseline Visit (Day 0). The minimum discontinuation period for wash-out is generally 5 half-lives of the medication or 7 consecutive evenings/nights medication-free prior to baseline, whichever is the longer period.
- During the Wash-out and Screening Phase, RLS symptoms must be present for at least 4 of the last 7 nights immediately prior to the Baseline Visit (e.g., any combination of evenings and /or nights for = 4 days).
- Subjects with a total score = 24 on the IRLS Rating Scale at baseline (Day 0).
- Subjects with RLS symptoms that cause significant sleep impairment based on clinical judgment and guided by subject response to Question 4 of the IRLS Rating Scale (e.g., ordinarily this will include a response of (3) severe or (4) very severe sleep disturbance) at the Baseline Visit OR RLS symptoms that cause severe/very severe discomfort in the limbs based on clinical judgment and guided by subject response to Question 1 of the IRLS Rating Scale (e.g., this will include a response of (3) severe or (4) very severe discomfort in limbs) at the Baseline Visit (Day 0).
- Subjects must be experiencing RLS symptoms requiring treatment at night-time.
- Subjects must have given written informed consent prior to any specific study procedures.

Exclusion criteria:

- Subjects suffering from augmentation and/ or 'end of treatment' rebound RLS symptoms at baseline (Day 0). Augmentation is defined as RLS symptoms that occurred while on treatment and occur earlier in the afternoon/evening than they did before, symptoms which are more severe than when not treated, symptoms which start after less time at rest than they did before treatment, or symptoms which involve other parts of the body, such as the arms or trunk. 'End of treatment' rebound describes worsening of symptoms from baseline that occur after pharmacological treatment is stopped.
- Subjects with a previous history of augmentation.
- Subjects who have exhibited intolerance to ropinirole or any other dopamine agonist.
- Subjects requiring treatment of daytime RLS symptoms (daytime defined as 10:00 hours until 17:00 hours).
- Signs of secondary RLS (e.g., end stage renal disease, iron deficient anaemia or pregnancy at Baseline Visit).

- Subjects with a serum ferritin level of < 10 mcg/L (ng/mL) at Screening Visit.
- Subjects who suffer from a primary sleep disorder other than RLS that may significantly affect the symptoms of RLS (e.g. narcolepsy, sleep terror disorder, sleepwalking disorder, breathing related sleep disorder).
- Subjects diagnosed with movement disorders (e.g., Parkinson's Disease, dyskinesias, and dystonias).
- Subjects who have medical conditions which could affect efficacy assessments or clinically significant or unstable medical conditions that present a safety concern. These may include, but are not limited to, the following disorders: diabetes, peripheral neuropathy, rheumatoid arthritis, fibromyalgia syndrome, symptomatic orthostatic hypotension, severe cardiovascular disease, hepatic or renal failure, pleuro-pulmonary fibrosis, major psychotic illness.
- Subjects having a clinically significant abnormal laboratory value, ECG, or physical examination findings not resolved by the time of the baseline examinations (Day 0). Abnormal 12-lead ECG findings include, but are not limited to, the following: myocardial ischemia, clinically significant conduction abnormalities, or clinically significant arrhythmias.
- Subjects with a diastolic blood pressure = 110mmHg or = 50mmHg or systolic blood pressure = 180mmHg or = 90mmHg at the Screening or Baseline Visit.
- Subjects with a history of alcohol or substance abuse within the past year.
- Subjects taking any medication known to induce drowsiness, affect RLS or sleep and which have not been discontinued prior to the Baseline Visit. These medications include the following:

Atypical and typical antipsychotics, anticonvulsants, opioids (including propoxyphene and oxycodone), anxiolytics, all sedatives/hypnotics (including benzodiazepines), lithium, oral neuroleptics, stimulants (including methylphenidate), dopamine agonists (including ropinirole), dopamine antagonists (e.g., typical neuroleptics, metoclopramide), levodopa/carbidopa, clonidine, and sedating antihistamines (e.g., chlorpheniramine, diphenhydramine, hydroxyzine) or any preparations containing these antihistamines.

The minimum discontinuation period is generally 5 half lives or 7 consecutive evenings/nights medication free, prior to baseline, whichever is the longer period. Exceptions to this general rule are: fluoxetine, monoamine oxidase inhibitors: 4 weeks.

For subjects entering the 40-week, open-label treatment phase, the GSK Medical Monitor can be contacted to discuss individual cases where adherence to the above may not have occurred.

- Withdrawal, introduction, or change in dose of hormone replacement therapy (HRT) and/or any drug known to substantially inhibit CYP1A2 (e.g., ciprofloxacin, cimetidine, fluvoxamine, HRT) or induce CYP1A2 (e.g., tobacco, omeprazole) within 7 days prior to enrolment. Subjects already on these agents may be enrolled, but must remain on stable doses of the agents from 7 days prior to enrolment through to the follow-up visit at the end of the study.
- Night workers or any others whose sleeping habits are incompatible with the study design, or who would be required to make significant changes to their bedtime during the course of the study.
- Participation in any clinical drug or device trial in the one month prior to the Baseline Visit.
- Subjects who, in the opinion of the investigator, would be non-compliant with the visit schedules or other study procedures.
- Women who have a positive pregnancy test or who are lactating.

Contacts and Locations

Locations

Australia, New South Wales

GSK Investigational Site

Camperdown, New South Wales, Australia, 2050

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Australia, South Australia

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Clayton, Victoria, Australia, 3168

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Investigators

Study Director:	GSK Clinical Trials	GlaxoSmithKline

More Information

Publications:

Diego García-Borreguero, Birgit Högl, Luigi Ferini-Strambi, John Winkelman, Christina Hill-Zabala, Afsaneh Asgharian, Richard Allen. Systematic evaluation of augmentation during treatment with ropinirole in restless legs syndrome (Willis-Ekbom disease): results from a prospective, multicenter study over 66

weeks. [Mov Disord]. 2012;27(2):277-283.

Responsible Party: GlaxoSmithKline
Study ID Numbers: ROR104836
Health Authority: Germany: Federal Institute for Drugs and Medical Devices

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Study Results

Participant Flow

Recruitment Details

Participants (par.) could enter the Open-Label (OL) phase at the end of the Double-Blind (DB) phase. If a par. did not complete the DB phase due to lack of efficacy, he/she could also be considered for entry into the OL phase if the investigator considered it appropriate and the par. met the protocol-defined criteria in describing lack of efficacy.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day
Open-label Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

26-Week Double-Blind Treatment Phase

	Double-blind Placebo	Double-blind Ropinirole IR	Open-label Ropinirole IR
Started	207 [1]	197	0

	Double-blind Placebo	Double-blind Ropinirole IR	Open-label Ropinirole IR
Completed	88	98	0
Not Completed	119	99	0
Did not complete phase; reason unknown	119	99	0

[1] Numbers of participants in the "Participant Flow" section are based on the Safety Population.

40-Week Open-Label Treatment Phase

	Double-blind Placebo	Double-blind Ropinirole IR	Open-label Ropinirole IR
Started	0	0	269 [1]
Completed	0	0	233
Not Completed	0	0	36
Adverse Event	0	0	20
Lost to Follow-up	0	0	1
Protocol Violation	0	0	2
Lack of Efficacy	0	0	9
Captured as Other	0	0	4

[1] 148 and 121 par. randomized to DB placebo and ropinirole IR, respectively, entered the OL phase.

Baseline Characteristics

Reporting Groups

	Description
Double-Blind Placebo	Matching placebo tablets
Double-Blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Baseline Measures

	Double-Blind Placebo	Double-Blind Ropinirole IR	Total
Number of Participants	207	197	404
Age, Continuous [1] [units: years] Mean (Standard Deviation)	55.9 (11.53)	56.5 (11.97)	56.2 (11.73)
Gender, Male/Female [2] [units: participants]			
Female	132	124	256
Male	75	73	148
Race/Ethnicity, Customized [3] [units: participants]			
White	204	197	401
Asian	2	0	2
Hawaiian or other Pacific Islander	1	0	1

[1] The Safety Population, comprised of all participants who received at least one dose of study medication, was used for all demographic characteristics.

[2] The Safety Population, comprised of all participants who received at least one dose of study

medication, was used for all demographic characteristics.

[3] The Safety Population, comprised of all participants who received at least one dose of study medication, was used for all demographic characteristics.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Mean Change From Baseline in the International Restless Legs Syndrome (IRLS) Rating Scale Total Score at Week 12 and Week 26
Measure Description	A 10-item, participant-reported scale covering different symptoms of the condition. Each item is scored from 0 to 4; 0 represents the absence of a problem and 4 reflects a very severe problem. The best and worst possible scores are 0 and 40, respectively; higher scores represent a greater severity of symptoms. A negative change from baseline indicates improvement, and a negative treatment difference indicates a benefit of Ropinirole IR over placebo. The primary assessment was made by calculating the difference in the average score obtained at Baseline with scores at Week 12 and then Week 26.
Time Frame	Baseline and Weeks 12 and 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets

	Description
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Mean Change From Baseline in the International Restless Legs Syndrome (IRLS) Rating Scale Total Score at Week 12 and Week 26 [units: points on a scale] Least Squares Mean (Standard Error)		
Week 12, n=165, 164	-12.1 (0.70)	-14.2 (0.71)
Week 26, n=119, 123	-13.4 (0.77)	-15.9 (0.76)

Statistical Analysis 1 for Mean Change From Baseline in the International Restless Legs Syndrome (IRLS) Rating Scale Total Score at Week 12 and Week 26

Groups	Double-blind Placebo, Double-blind Ropinirole IR
Method	Other [Repeated Measures Mixed Model]
P-Value	0.039

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

P-value is for Week 12.

Other relevant information, such as adjustments or degrees of freedom:

Adjusted for baseline IRLS Rating Scale total score, treatment group, visit, visit by treatment group interaction, and center group.

Statistical Analysis 2 for Mean Change From Baseline in the International Restless Legs Syndrome (IRLS) Rating Scale Total Score at Week 12 and Week 26

Groups	Double-blind Placebo, Double-blind Ropinirole IR
Method	Other [Repeated Measures Mixed Model]
P-Value	0.023

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

P-value is for Week 26.

Other relevant information, such as adjustments or degrees of freedom:

Adjusted for baseline IRLS Rating Scale total score, treatment group, visit, visit by treatment group interaction, and center group.

2. Primary Outcome Measure:

Measure Title	Number of Participants With Clinically Meaningful Augmentation and Early Morning Rebound (EMR) Cases
Measure Description	Clinically meaningful augmentation and early morning rebound (EMR) were assessed and confirmed by an independent Adjudication Board. EMR describes the development of RLS symptoms during the early morning, following therapeutic intervention. EMR is differentiated from augmentation, in which the earlier onset of symptoms occurs in the

	evening.
Time Frame	During 15-month study duration at scheduled (Weeks 16, 20, 26, or early withdrawal for DB phase; Weeks 39, 47, 55, 63, 67, or early withdrawal for the OL phase) and unscheduled (26-week DB phase and 40-week OL phase) visits
Safety Issue?	Yes

Analysis Population Description

Safety Population: all participants who received at least one dose of study medication

Reporting Groups

	Description
Overall Study	
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day
Open-label Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Overall Study	Double-blind Placebo	Double-blind Ropinirole IR	Open-label Ropinirole IR
Number of Participants Analyzed	404	207	197	269
Number of Participants With Clinically Meaningful Augmentation and Early Morning Rebound (EMR) Cases				

	Overall Study	Double-blind Placebo	Double-blind Ropinirole IR	Open-label Ropinirole IR
[units: participants]				
Confirmed augmentation	15	1	7	8
Clinically meaningful augmentation	11	1	5	5
Confirmed EMR	7	1	4	2

3. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in the International RLS (IRLS) Rating Scale Total Score at Weeks 1, 4, 8, 16, and 20
Measure Description	A 10-item, participant-reported scale covering different RLS symptoms. Each item is scored from 0 to 4; 0 represents the absence of a problem and 4 reflects a very severe problem. The best and worst possible scores are 0 and 40, respectively; higher scores represent a greater severity of symptoms. The primary assessment from this study was made by calculating the difference in the average score obtained at Baseline with scores at Weeks 1, 4, 8, 16, and 20. Scores were adjusted for baseline IRLS total score, treatment group, visit, visit by treatment group interaction, and center group.
Time Frame	Baseline and Weeks 1, 4, 8, 16, and 20
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Mean Change From Baseline in the International RLS (IRLS) Rating Scale Total Score at Weeks 1, 4, 8, 16, and 20 [units: points on a scale] Least Squares Mean (Standard Error)		
Week 1, n=198, 194	-5.5 (0.52)	-7.8 (0.52)
Week 4, n=183, 180	-10.5 (0.60)	-13.6 (0.60)
Week 8, n=168, 170	-13.0 (0.66)	-15.3 (0.66)
Week 16, n=137, 144	-12.6 (0.75)	-15.0 (0.74)
Week 20, n=125, 132	-12.3 (0.78)	-15.7 (0.77)

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Domains of the 12-item Medical Outcomes Study (MOS-12) Sleep Scale at Weeks 12 and 26

Measure Description	The MOS-12 Sleep Scale is a comprehensive battery, which measures specific aspects of sleep in participants that may have varying co-morbidities, and, as a result, is appropriate for a medically diverse participant population. Domain values are presented on a 0-100 scale, where a higher score means a greater degree of the attribute implied by the scale name. Scores were adjusted for baseline MOS sleep scale domain value, treatment group, visit, visit by treatment interaction, and center group.
Time Frame	Baseline and Weeks 12 and 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Change From Baseline in the Domains of the 12-item Medical Outcomes Study (MOS-12) Sleep Scale at Weeks 12 and		

	Double-blind Placebo	Double-blind Ropinirole IR
26 [units: points on a scale] Least Squares Mean (Standard Error)		
Sleep disturbance, Week 12, n=153, 143	-15.0 (1.62)	-24.0 (1.67)
Sleep disturbance, Week 26, n=105, 97	-16.4 (1.80)	-24.6 (1.87)
Sleep adequacy, Week 12, n=153, 143	15.0 (1.91)	22.8 (1.98)
Sleep adequacy, Week 26, n=105, 97	14.9 (2.16)	26.0 (2.25)
Daytime somnolence, Week 12, n=153, 143	-7.5 (1.28)	-11.4 (1.33)
Daytime somnolence, Week 26, n=105, 97	-9.1 (1.59)	-11.4 (1.65)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in Sleep Quantity, a Domain of the 12-item Medical Outcomes Study (MOS-12) Sleep Scale, at Weeks 12 and 26
Measure Description	The MOS-12 Sleep Scale is a comprehensive battery, which measures specific aspects of sleep in participants that may have varying co-morbidities, and, as a result, is appropriate for a medically diverse participant population.Scores were adjusted for baseline MOS sleep scale domain value, treatment group, visit, visit by treatment interaction, and center group.
Time Frame	Baseline and Weeks 12 and 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Change From Baseline in Sleep Quantity, a Domain of the 12-item Medical Outcomes Study (MOS-12) Sleep Scale, at Weeks 12 and 26 [units: hours] Least Squares Mean (Standard Error)		
Week 12, n=153, 143	0.5 (0.10)	0.7 (0.11)
Week 26, n=105, 97	0.5 (0.11)	0.7 (0.11)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Johns Hopkins RLS Quality of Life (RLS QoL) Questionnaire Overall Life Impact Score at Weeks 12 and 26

Measure Description	The Johns Hopkins RLS QoL Questionnaire is a disease-specific instrument that assesses the impact of RLS on the daily life, emotional well-being, social life, and work life of participants. The overall life impact score for the John Hopkins RLS QoL scale ranges from a lowest possible score of 0 to a highest possible score of 100. Higher scores represent better quality of life. Scores were adjusted for baseline RLS Quality of Life score, treatment group, visit, visit by treatment interaction, and center group.
Time Frame	Baseline and Weeks 12 and 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Change From Baseline in the Johns Hopkins RLS Quality of Life (RLS QoL) Questionnaire Overall Life Impact Score at		

	Double-blind Placebo	Double-blind Ropinirole IR
Weeks 12 and 26 [units: points on a scale] Least Squares Mean (Standard Error)		
Week 12, n=149, 141	14.0 (1.29)	18.0 (1.33)
Week 26, n=103, 94	16.5 (1.35)	18.5 (1.41)

7. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Domains of the MOS 36-item Short Form Health Survey (SF-36) at Weeks 12 and 26
Measure Description	The MOS SF-36 is a generic QoL instrument measuring functional status and well-being. Positive change from baseline for all domains indicates improvement. For all MOS SF-36 domains, the minimum and maximum scores are 0 and 100, respectively, for the transformed scale. Scores were adjusted for baseline domain score, treatment group, visit, visit by treatment interaction, and center group.
Time Frame	Baseline and Weeks 12 and 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets

	Description
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Change From Baseline in the Domains of the MOS 36-item Short Form Health Survey (SF-36) at Weeks 12 and 26 [units: points on a scale] Least Squares Mean (Standard Error)		
Bodily pain, Week 12, n=149, 142	12.3 (1.72)	14.4 (1.76)
Bodily pain, Week 26, n=104, 94	13.3 (2.01)	14.0 (2.11)
General health, Week 12, n=149, 142	3.0 (1.08)	4.5 (1.11)
General health, Week 26, n=104, 94	2.6 (1.31)	4.1 (1.37)
Mental health, Week 12, n=149, 142	5.0 (1.22)	7.6 (1.26)
Mental health, Week 26, n=104, 94	4.6 (1.25)	6.2 (1.31)
Physical functioning, Week 12, n=149, 142	2.4 (1.22)	5.5 (1.25)
Physical functioning, Week 26, n=104, 94	3.5 (1.48)	2.6 (1.54)
Role emotional, Week 12, n=149, 142	5.1 (1.62)	7.0 (1.67)
Role emotional, Week 26, n=104, 94	5.9 (1.66)	6.6 (1.74)

	Double-blind Placebo	Double-blind Ropinirole IR
Role physical, Week 12, n=149, 142	5.2 (1.66)	7.7 (1.71)
Role physical, Week 26, n=104, 94	7.5 (1.85)	6.7 (1.94)
Social functioning, Week 12, n=149, 142	6.3 (1.58)	9.8 (1.62)
Social functioning, Week 26, n=104, 94	7.1 (1.56)	8.8 (1.63)
Vitality, Week 12, n=149, 142	8.0 (1.37)	9.3 (1.41)
Vitality, Week 26, n=104, 94	6.0 (1.54)	9.2 (1.61)

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Score of Much/Very Much Improved on the Clinical Global Impression-Global Improvement (CGI-I) Scale at Weeks 1, 12 and 26
Measure Description	The CGI-I is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-I allows the investigator to rate the participant's global improvement or worsening compared with the condition at Baseline (Day 0). The scale is rated from 1-7 (1 = very much improved; 7 = very much worse). Typically, a participant with a score of 1 or 2 (much improved) is considered a responder.
Time Frame	Weeks 1, 12 and 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	192	192
Percentage of Participants With a Score of Much/Very Much Improved on the Clinical Global Impression-Global Improvement (CGI-I) Scale at Weeks 1, 12 and 26 [units: percentage of participants]		
Week 1, n=192, 192	39	50
Week 12, n=165, 160	86	109
Week 26, n=112, 108	72	91

9. Secondary Outcome Measure:

Measure Title	Number of Participants Withdrawing Due to Lack of Efficacy During the First 26 Weeks of the Study
Measure Description	Lack of efficacy is defined as up to a 10% improvement in the IRLS Rating Scale total score from the participant's Baseline value and at least 12 weeks of treatment during the double-blind phase.

Time Frame	Baseline to Week 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Number of Participants Withdrawing Due to Lack of Efficacy During the First 26 Weeks of the Study [units: participants]	2	3

10. Secondary Outcome Measure:

Measure Title	Number of Participants Rated as Normal or Borderline Ill on the CGI Severity of Illness (CGI-S) Scale at Week 26
Measure Description	The CGI-S scale is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-S allows

	the investigator to rate the severity of the participant's illness considering their total clinical experience with the subject population being studied and on all information available at the time of rating. The scale is rated from 1-7 (1 = normal, not at all ill; 2 = borderline ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severly ill; 7 = among the most extremely ill participants).
Time Frame	Week 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available. Data are presented for the participants still in the study and assessed at Week 26, which is less than those randomised at baseline.

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	112	108
Number of Participants Rated as Normal or Borderline Ill on the CGI Severity of Illness (CGI-S) Scale at Week 26 [units: participants]	50	50

11. Secondary Outcome Measure:

Measure Title	Median Time to First CGI-I Response of Much/Very Much Improved During the Double-blind Phase
Measure Description	The median time to first CGI-I response of much/very much improved was calculated. The CGI-I is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-I allows the investigator to rate the participant's global improvement or worsening compared with the condition at Baseline (Day 0). The scale is rated from 1-7 (1 = very much improved; 7 = very much worse). Typically, a participant with a score of 1 or 2 (much improved) is considered a responder.
Time Frame	Baseline to Week 26
Safety Issue?	No

Analysis Population Description

Intention-to-Treat (ITT) Population: all randomised participants who received at least one dose of study medication, and for whom at least one valid post-baseline efficacy assessment was available

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	205	196
Median Time to First CGI-I Response of Much/Very Much Improved During the Double-blind Phase [units: days] Median (95% Confidence Interval)	28 (22 to 33)	21 (14 to 21)

12. Secondary Outcome Measure:

Measure Title	Number of Participants With a Score of Much/Very Much Improved on the CGI-I Scale at Week 67
Measure Description	The CGI-I is a psychometric instrument that is used to measure general clinical status in a variety of disease states. The CGI-I allows the investigator to rate the participant's global improvement or worsening compared with the condition at Baseline (Day 0). The scale is rated from 1-7 (1 = very much improved; 7 = very much worse). Typically, a participant with a score of 1 or 2 (much improved) is considered a responder.
Time Frame	Week 67
Safety Issue?	No

Analysis Population Description

Open-Label (OL) ITT Population: all participants who were enrolled into the OL Phase of the study, received at least one dose of OL study medication, and had a baseline IRLS total score and on-treatment IRLS assessment. Data are presented for participants still in the study and assessed at Week 26, which is less than those randomized at baseline.

Reporting Groups

	Description
Open-label Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Open-label Ropinirole IR
Number of Participants Analyzed	200
Number of Participants With a Score of Much/Very Much Improved on the CGI-I Scale at Week 67 [units: participants]	184

13. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in the IRLS Rating Scale Total Score at Week 67
Measure Description	A 10-item, participant-reported scale covering different symptoms of the condition. Each item is scored from 0 to 4, with 0 representing the absence of a problem and 4 reflecting a very severe problem. The best and worst possible scores are 0 and 40, respectively. The primary assessment was made by calculating the difference in the average score obtained at Baseline with score at Week 67.
Time Frame	Baseline and Week 67
Safety Issue?	No

Analysis Population Description

Open-Label ITT Population: all participants who were enrolled into the Open-Label Phase of the study, received at least one dose of Open-Label study medication, and had a baseline IRLS total score and on-treatment IRLS assessment. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Open-label Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Measured Values

	Open-label Ropinirole IR
Number of Participants Analyzed	268
Mean Change From Baseline in the IRLS Rating Scale Total Score at Week 67 [units: points on a scale] Mean (Standard Deviation)	-20.4 (8.36)

14. Post-Hoc Outcome Measure:

Measure Title	Post-hoc Analysis of Mean Change From Baseline in the International Restless Legs Syndrome (IRLS) Rating Scale Total Score at Week 12 and Week 26, Exploring the Impact of Center Group on Treatment Effect
Measure Description	A post-hoc analysis of the primary outcome measure, exploring the variation in treatment effects across center groups by excluding those with the most extreme treatment effects, was conducted. Centers were grouped into five center groups.
Time Frame	Baseline and Weeks 12 and 26

Safety Issue?	No

Analysis Population Description

ITT Population excluding the two center groups with the most extreme treatment effects. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Double-Blind Placebo participants (receiving matching placebo tablets) who were not in the center groups with the highest or lowest treatment effects
Double-blind Ropinirole IR	Double-Blind Ropinirole participants (receiving Ropinirole IR [immediate release] tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day) who were not in the center groups with the highest or lowest treatment effects

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	136	134
Post-hoc Analysis of Mean Change From Baseline in the International Restless Legs Syndrome (IRLS) Rating Scale Total Score at Week 12 and Week 26, Exploring the Impact of Center Group on Treatment Effect [units: Points on a scale] Least Squares Mean (Standard Error)		
Week 12, n=136, 134	-12.2 (0.78)	-13.8 (0.79)
Week 26, n=103, 105	-14.0 (0.84)	-15.7 (0.83)

15. Post-Hoc Outcome Measure:

Measure Title	Post-hoc Analysis of Percentage of Participants With a Score of Much/Very Much Improved on the Clinical Global Impression-Global Improvement (CGI-I) Scale at Weeks 12 and 26, Exploring the Impact of Center Group on Treatment Effect
Measure Description	A post-hoc analysis of CGI-I, exploring the variation in treatment effects across center groups by excluding the same two center groups as in the IRLS post-hoc analysis, was conducted. Centers were grouped into five center groups.
Time Frame	Weeks 12 and 26
Safety Issue?	No

Analysis Population Description

ITT Population excluding the same two center groups as in the IRLS post-hoc analysis. Analysis is based on the observed cases for each visit.

Reporting Groups

	Description
Double-blind Placebo	Double-Blind Placebo participants (receiving matching placebo tablets) who were not excluded from the IRLS post-hoc analysis
Double-blind Ropinirole IR	Double-Blind Ropinirole participants (receiving Ropinirole IR [immediate release] tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day) who were not excluded from the IRLS post-hoc analysis

Measured Values

	Double-blind Placebo	Double-blind Ropinirole IR
Number of Participants Analyzed	136	134
Post-hoc Analysis of Percentage of Participants With a Score of Much/Very Much Improved on the Clinical Global Impression-Global Improvement (CGI-I) Scale at Weeks 12 and 26, Exploring the Impact of Center Group on Treatment Effect [units: Number of responders]		
Week 12, n=136, 134	75	93
Week 26, n=99, 96	63	82

Reported Adverse Events

Reporting Groups

	Description
Double-blind Placebo	Matching placebo tablets
Double-blind Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.25 mg, 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day
Open-Label Ropinirole IR	Ropinirole IR (immediate release) tablets containing ropinirole hydrochloride equivalent to 0.5 mg, 1.0 mg, or 2.0 mg of the active drug substance, taken once a day

Serious Adverse Events

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
Total # participants affected/at risk	6/207 (2.9%)	6/197 (3.05%)	11/269 (4.09%)
Ear and labyrinth disorders			
Vertigo † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Gastrointestinal disorders			
Abdominal pain † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			
Abdominal pain upper † [A]			
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			
Peptic ulcer † [A]			
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			
General disorders			

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
Chest pain † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Hepatobiliary disorders			
Cholelithiasis † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Gallbladder disorder † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			
Infections and infestations			
Appendicitis † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			
Post procedural infection † [A]			
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
Pyelonephritis † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			
Injury, poisoning and procedural complications			
Femoral neck fracture † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Head injury † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Joint dislocation † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			
Musculoskeletal and connective tissue disorders			
Bursa calcification † [A]			
# participants affected/at	0/207 (0%)	0/197 (0%)	1/269 (0.37%)

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
risk			
# events			
Myalgia † [A]			
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			
Osteoarthritis † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Osteonecrosis † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Rotator cuff syndrome † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma † [A]			

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			
Uterine cancer † [A]			
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			
Nervous system disorders			
Brain stem ischaemia † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Cerebral infarction † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			
Syncope † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Reproductive system and breast disorders			

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
Fallopian tube cyst † [A]			
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			
Ovarian cyst † [A]			
# participants affected/at risk	0/207 (0%)	1/197 (0.51%)	0/269 (0%)
# events			
Ovarian cyst torsion † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			
Postmenopausal haemorrhage † [A]			
# participants affected/at risk	0/207 (0%)	0/197 (0%)	1/269 (0.37%)
# events			
Vascular disorders			
Hypertension † [A]			
# participants affected/at risk	1/207 (0.48%)	0/197 (0%)	0/269 (0%)
# events			

† Indicates events were collected by systematic assessment.

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Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
Total # participants affected/at risk	71/207 (34.3%)	123/197 (62.44%)	122/269 (45.35%)
Gastrointestinal disorders			
Diarrhea †[A]			
# participants affected/at risk	5/207 (2.42%)	10/197 (5.08%)	3/269 (1.12%)
# events			
Nausea †[A]			
# participants affected/at risk	16/207 (7.73%)	83/197 (42.13%)	67/269 (24.91%)
# events			
Vomiting †[A]			
# participants affected/at risk	0/207 (0%)	22/197 (11.17%)	13/269 (4.83%)
# events			
General disorders			
Fatigue †[A]			
# participants affected/at risk	14/207 (6.76%)	28/197 (14.21%)	29/269 (10.78%)

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
# events			
Infections and infestations			
Nasopharyngitis † [A]			
# participants affected/at risk	14/207 (6.76%)	21/197 (10.66%)	33/269 (12.27%)
# events			
Musculoskeletal and connective tissue disorders			
Back pain † [A]			
# participants affected/at risk	11/207 (5.31%)	7/197 (3.55%)	9/269 (3.35%)
# events			
Nervous system disorders			
Dizziness † [A]			
# participants affected/at risk	6/207 (2.9%)	20/197 (10.15%)	16/269 (5.95%)
# events			
Headache † [A]			
# participants affected/at risk	23/207 (11.11%)	29/197 (14.72%)	20/269 (7.43%)

	Double-blind Placebo	Double-blind Ropinirole IR	Open-Label Ropinirole IR
# events			
Somnolence † [A]			
# participants affected/at risk	4/207 (1.93%)	9/197 (4.57%)	14/269 (5.2%)
# events			
Psychiatric disorders			
Insomnia † [A]			
# participants affected/at risk	5/207 (2.42%)	12/197 (6.09%)	1/269 (0.37%)
# events			

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

GSK agreements may vary with individual investigators, but will not prohibit any investigator from publishing. GSK supports the publication of results from all centers of a multi-center trial but requests that reports based on single-site data not precede the primary publication of the entire clinical trial.

Limitations and Caveats:

Results Point of Contact:

Name/Official Title: GSK Response Center

Organization: GlaxoSmithKline

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