EU Clinical Trials Register

Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, 52-Week Phase II Study to Evaluate the Efficacy of Intravenous RO7046015 (PRX002) in Participants with Early Parkinson's Disease with a 6-Year all-Participants-on-Treatment Extension (PASADENA)

Summary

EudraCT number	2017-000087-15
Trial protocol	DE AT ES FR
Global end of trial date	

Results information

Result version number	v1
This version publication date	12 December 2020
First version publication date	12 December 2020

Trial information

Trial identification

Sponsor protocol code	BP39529

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03100149
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, ch-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	27 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of prasinezumab versus placebo at Week 52 in participants with early Parkinson's Disease (PD, [H&Y Stages I-II]) who were untreated or treated with MAO-B inhibitors since baseline as measured by change from baseline on the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (sum of Parts I, II and III).

Protection of trial subjects:

All study subjects were required to read and sign and Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 June 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	France: 65
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Spain: 50
Country: Number of subjects enrolled	United States: 160
Worldwide total number of subjects	316
EEA total number of subjects	156

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	205
From 65 to 84 years	111
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 316 were randomized with a 1:1:1 allocation between the treatment groups (Placebo, Low-Dose prasinezumab and High-Dose prasinezumab)

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Placebo

Arm description:

Participants received placebo as intravenous (IV) infusion every four weeks (Q4W) up to 52 weeks in Part 1.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was administered by intravenous (IV) infusion once every for weeks (Q4W) to all participants in the indicated arm.

Arm title	Part 1: RO7046015 Low Dose

Arm description:

Participants received RO7046015 at a low dose level (1500 mg; for all body weights) as an IV infusion Q4W up to 52 weeks in Part 1.

Arm type	Experimental
Investigational medicinal product name	RO7046015
Investigational medicinal product code	
Other name	PRX002; prasinezumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

RO7046015 was administered by IV infusion Q4W at dose of 1500 mg to all participants in the indicated arm.

Arm title	Part 1: RO7046015 High Dose

Arm description:

Participants received RO7046015 at a high dose level (3500 mg for body weight <65 kilogram (kg) or 4500 mg for body weight >=65 kg) as an IV infusion Q4W up to 52 weeks in Part 1.

Arm type	Experimental

Investigational medicinal product name	RO7046015
Investigational medicinal product code	
Other name	PRX002; prasinezumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

RO7046015 was administered by IV infusion Q4W at dose of 4500 milligrams (mg) for participants with body-weight greater than or equal to ($\geq$) 65 kilograms (kg) or 3500 mg for participants with body-weight less than (<) 65 kg.

Number of subjects in period 1	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose
Started	105	105	106
Completed	105	101	104
Not completed	0	4	2
PATIENT MOVING OUT OF THE COUNTRY	-	-	1
Withdrawal By Subject	-	3	1
Adverse event, non-fatal	-	1	-

Baseline characteristics

Reporting groups

Reporting group title	Part 1: Placebo
Reporting group description:	
Participants received placebo as intravenous (IV) infusion every four weeks (Q4W) up to 52 weeks in Part 1.	
Reporting group title	Part 1: RO7046015 Low Dose
Reporting group description:	
Participants received RO7046015 at a low dose level (1500 mg; for all body weights) as an IV infusion Q4W up to 52 weeks in Part 1.	
Reporting group title	Part 1: RO7046015 High Dose
Reporting group description:	
Participants received RO7046015 at a high dose level (3500 mg for body weight <65 kilogram (kg) or 4500 mg for body weight >=65 kg) as an IV infusion Q4W up to 52 weeks in Part 1.	

Reporting group values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose
Number of subjects	105	105	106
Age Categorical			
Units: Subjects			
Preterm newborn infants (gestational age <37 weeks)	0	0	0
Newborns(0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	72	68	65
From 65-84 years	33	37	41
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	59.9	60.3	59.4
standard deviation	± 8.7	± 8.8	± 9.8
Sex: Female, Male			
Units: Subjects			
Male	71	71	71
Female	34	34	35
Race (NIH/OMB)			
Units: Subjects			
Asian	1	0	0
Black or African American	0	2	0
White	91	83	89
Unknown	13	20	17

Reporting group values	Total		
Number of subjects	316		
Age Categorical			
Units: Subjects			

Preterm newborn infants (gestational age <37 weeks)	0		
Newborns(0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	205		
From 65-84 years	111		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Subjects			
Male	213		
Female	103		
Race (NIH/OMB)			
Units: Subjects			
Asian	1		
Black or African American	2		
White	263		
Unknown	50		

End points

End points reporting groups

Reporting group title	Part 1: Placebo
Reporting group description:	
Participants received placebo as intravenous (IV) infusion every four weeks (Q4W) up to 52 weeks in Part 1.	
Reporting group title	Part 1: RO7046015 Low Dose
Reporting group description:	
Participants received RO7046015 at a low dose level (1500 mg; for all body weights) as an IV infusion Q4W up to 52 weeks in Part 1.	
Reporting group title	Part 1: RO7046015 High Dose
Reporting group description:	
Participants received RO7046015 at a high dose level (3500 mg for body weight <65 kilogram (kg) or 4500 mg for body weight >=65 kg) as an IV infusion Q4W up to 52 weeks in Part 1.	

Primary: Change From Baseline in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 52

End point title	Change From Baseline in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 52

End point description:

The MDS-UPDRS is a multimodal scale consisting of four subscales. Part I assesses non-motor experiences of daily living. Part IA contains 6 questions and are assessed by the examiner. Part IB contains 7 questions on non-motor experiences of daily living which are a part of the self-administered Patient Questionnaire completed by the participant. Part II assesses motor experiences of daily living. There are 13 questions which are a part of the self-administered Patient Questionnaire completed by the participant. Part III assesses the motor signs of Parkinson's Disease (PD) and is administered by the rater. This part contains 33 scores that are based on 18 items. There are 4 subscores in Part III: Bradykinesia, Rigidity, Resting tremors and Axial symptoms. For each question a numeric score is assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. Composite scores (for each Part and total) were determined by summing the numeric values of each question.

End point type	Primary

End point timeframe:

From baseline to Week 52

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	73	
Units: Units on a scale				
least squares mean (standard error)	9.37 (± 1.221)	7.35 (± 1.225)	8.75 (± 1.234)	

Statistical analyses

Statistical analysis title	MDS-UPDRS Total - Low-Dose group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2385
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-2.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-4.21
upper limit	0.18
Variability estimate	Standard error of the mean
Dispersion value	1.71

Statistical analysis title	MDS-UPDRS Total - High-Dose group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7169
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.62
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.82
upper limit	1.58
Variability estimate	Standard error of the mean
Dispersion value	1.71

Secondary: Change From Baseline in the MDS-UPDRS Part IA, Part IB, Part I total, Part II total, Part III total and Part III Subscores

End point title	Change From Baseline in the MDS-UPDRS Part IA, Part IB, Part I total, Part II total, Part III total and Part III Subscores

End point description:

The MDS-UPDRS is a multimodal scale consisting of four subscales. Part I assesses non-motor experiences of daily living. Part IA contains 6 questions and are assessed by the examiner. Part IB contains 7 questions on non-motor experiences of daily living which are a part of the self-administered Patient Questionnaire completed by the participant. Part II assesses motor experiences of daily living. There are 13 questions which are a part of the self-administered Patient Questionnaire completed by the participant. Part III assesses the motor signs of PD and is administered by the rater. This part contains 33 scores that are based on 18 items. There are 4 subscores in Part III: Bradykinesia, Rigidity, Resting tremors and Axial symptoms. For each question a numeric score is assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. Composite scores (for each Part and total) were determined by summing the numeric values of each question.

End point type	Secondary
End point timeframe:	
From baseline to Week 52	

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	74	73	
Units: Units on a scale				
least squares mean (standard error)				
Part IA	-0.19 (± 0.119)	-0.27 (± 0.119)	-0.10 (± 0.121)	
Part IB	0.94 (± 0.247)	0.90 (± 0.248)	0.96 (± 0.251)	
Part I total	0.77 (± 0.295)	0.59 (± 0.297)	0.89 (± 0.300)	
Part II total	2.75 (± 0.373)	3.09 (± 0.375)	2.69 (± 0.376)	
Part III total	5.57 (± 0.897)	3.69 (± 0.900)	4.55 (± 0.911)	
Part III subscore - rigidity	0.61 (± 0.263)	0.70 (± 0.265)	0.86 (± 0.268)	
Part III subscore - bradykinesia	2.79 (± 0.556)	1.72 (± 0.560)	2.35 (± 0.565)	
Part III subscore - resting tremor	1.20 (± 0.231)	0.59 (± 0.233)	0.79 (± 0.234)	
Part III subscore - axial symptoms	0.19 (± 0.077)	0.11 (± 0.078)	0.18 (± 0.079)	

Statistical analyses

Statistical analysis title	Part IA - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6116 [1]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.08
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.3
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.165

Notes:

[1] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part IA - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose

Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6188 [2]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	0.08
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.13
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.165

Notes:

[2] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part IB - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9062 [3]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.04
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.48
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.345

Notes:

[3] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part IB - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9621 [4]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	0.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.43
upper limit	0.46

Variability estimate	Standard error of the mean
Dispersion value	0.347

Notes:

[4] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part I Total - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.651 [5]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.19
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.71
upper limit	0.34
Variability estimate	Standard error of the mean
Dispersion value	0.411

Notes:

[5] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part I Total - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7709 [6]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	0.12
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.41
upper limit	0.65
Variability estimate	Standard error of the mean
Dispersion value	0.413

Notes:

[6] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part II Total - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose

Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5177 [7]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	0.34
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.33
upper limit	1.01
Variability estimate	Standard error of the mean
Dispersion value	0.523

Notes:

[7] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part II Total - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9095 [8]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.06
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.73
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	0.523

Notes:

[8] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Total - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1354 [9]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-1.88
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-3.49
upper limit	-0.27

Variability estimate	Standard error of the mean
Dispersion value	1.255

Notes:

[9] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Total - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4217 [10]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-1.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.64
upper limit	0.61
Variability estimate	Standard error of the mean
Dispersion value	1.262

Notes:

[10] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Rigidity Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8053 [11]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	0.09
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.38
upper limit	0.56
Variability estimate	Standard error of the mean
Dispersion value	0.369

Notes:

[11] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Rigidity High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose

Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.497 [12]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	0.25
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.22
upper limit	0.73
Variability estimate	Standard error of the mean
Dispersion value	0.37

Notes:

[12] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Bradykinesia Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1703 [13]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-1.07
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.07
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.779

Notes:

[13] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Bradykinesia High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5729 [14]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.44
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.45
upper limit	0.56

Variability estimate	Standard error of the mean
Dispersion value	0.782

Notes:

[14] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Resting Tremor Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0628 [15]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.61
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.02
upper limit	-0.19
Variability estimate	Standard error of the mean
Dispersion value	0.324

Notes:

[15] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Resting Tremor High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2125 [16]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.41
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.82
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.325

Notes:

[16] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Axial Symptoms Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose

Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4577 [17]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.08
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.22
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.108

Notes:

[17] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	Part III Subscore: Axial Symptoms High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9182 [18]
Method	Mixed models analysis
Parameter estimate	LS Means Difference
Point estimate	-0.01
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.15
upper limit	0.13
Variability estimate	Standard error of the mean
Dispersion value	0.109

Notes:

[18] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Change From Baseline in Dopamine Transporter Imaging With Single Photon Emission Computed Tomography (DaT-SPECT) in the Ipsilateral Putamen

End point title	Change From Baseline in Dopamine Transporter Imaging With Single Photon Emission Computed Tomography (DaT-SPECT) in the Ipsilateral Putamen

End point description:

DaT-SPECT (dopamine transporter imaging with single photon emission computed tomography) is a dopamine transporter SPECT imaging that uses a radioactive agent called 123^I-ioflupane to show the distribution of the dopamine transporters in the striatum. The change in DaT-SPECT uptake values in the ipsilateral putamen to the most clinical affected side, were analyzed.

End point type	Secondary

End point timeframe:

From baseline to Week 52

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	100	104	
Units: Images				
least squares mean (standard error)	-0.08 (± 0.018)	-0.10 (± 0.018)	-0.11 (± 0.018)	

Statistical analyses

Statistical analysis title	DaT-SPECT - Low-Dose group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3582 [19]
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	-0.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.05
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.02

Notes:

[19] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	DaT-SPECT - High-Dose group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1955 [20]
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	-0.03
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.06
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.02

Notes:

[20] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Change from Baseline in Montreal Cognition Assessment (MoCA) Total Score

End point title	Change from Baseline in Montreal Cognition Assessment (MoCA) Total Score
End point description:	
The Montreal Cognitive Assessment (MoCA) is a rapid screening that was developed to be more sensitive to participants presenting with mild cognitive complaints. It briefly assesses short term and working memory, visuospatial abilities, executive function, attention, concentration, language and orientation.	
End point type	Secondary
End point timeframe:	
From baseline to Week 52	

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	100	103	
Units: Units on a scale				
least squares mean (standard error)	0.07 (± 0.177)	0.30 (± 0.181)	0.51 (± 0.178)	

Statistical analyses

Statistical analysis title	MoCA - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3611 [21]
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	0.22
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.09
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	0.245

Notes:

[21] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	MoCA - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose

Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0727 [22]
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	0.44
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.13
upper limit	0.75
Variability estimate	Standard error of the mean
Dispersion value	0.243

Notes:

[22] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Change from Baseline in Clinical Global Impression of Improvement (CGI-I) Score

End point title	Change from Baseline in Clinical Global Impression of Improvement (CGI-I) Score

End point description:

The CGI-I is a measure of disease severity at baseline and is rated on a 7-point scale,with the severity (CGI-I) of illness scale using a range of responses from 1 (normal, not at all ill) through to 7 (amongst the most extremely ill patients).

End point type	Secondary

End point timeframe:

From baseline to Week 52

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	36	35	
Units: Percentage of participants				
number (not applicable)	56.6	50.0	48.6	

Statistical analyses

Statistical analysis title	CGI-I - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4265 [23]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.77

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.5
upper limit	1.18

Notes:

[23] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	CGI-I - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4063 [24]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.76
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.49
upper limit	1.16

Notes:

[24] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Change from Baseline in Patient Global Impression of Change (PGIC) Score

End point title	Change from Baseline in Patient Global Impression of Change (PGIC) Score

End point description:

The Patient Global Impression of Change (PGIC) is intended as a measure of change in health state from the patient's perspective. PGIC scores range from 1 (very much improved) through to 7 (very much worse).

End point type	Secondary

End point timeframe:

From baseline to Week 52

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43	37	38	
Units: Percentage of participants				
number (not applicable)	58.1	50.7	53.5	

Statistical analyses

Statistical analysis title	PGIC - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3847 [25]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.48
upper limit	1.15

Notes:

[25] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	PGIC - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7055 [26]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.88
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.57
upper limit	1.36

Notes:

[26] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Change from Baseline in Schwab and England Activity of Daily Living (SE-ADL) Score

End point title	Change from Baseline in Schwab and England Activity of Daily Living (SE-ADL) Score

End point description:

The SE-ADL is a single item scale assessing Activities of Daily Living on a scale ranging from 0% (bedridden) to 100% (completely independent), using 10% intervals.

End point type	Secondary

End point timeframe:

From baseline to Week 52

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	102	103	
Units: Units on a scale				
least squares mean (standard error)	-1.83 (± 0.644)	-2.56 (± 0.650)	-2.50 (± 0.647)	

Statistical analyses

Statistical analysis title	SE-ADL - Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	206
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4142 [27]
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	-0.73
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.87
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.888

Notes:

[27] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	SE-ADL - High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	207
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4486 [28]
Method	ANCOVA
Parameter estimate	LS Means Difference
Point estimate	-0.67
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-1.81
upper limit	0.47
Variability estimate	Standard error of the mean
Dispersion value	0.885

Notes:

[28] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Time to Worsening in Motor or Non-Motor Symptoms

End point title	Time to Worsening in Motor or Non-Motor Symptoms
End point description:	
This outcome measure is defined as the time to between first dose of study medication and the date when the patient increase in MDS-UPDRS Part I of 3 or more points, or in MDS-UPDRS Part II of 3 or more points, whichever comes first.	
End point type	Secondary
End point timeframe:	
From baseline to Week 52	

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	105	106	
Units: Days				
median (confidence interval 80%)	174.0 (168.0 to 225.0)	169.0 (117.0 to 173.0)	170.0 (168.0 to 222.0)	

Statistical analyses

Statistical analysis title	Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3769 [29]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.94
upper limit	1.42

Notes:

[29] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1658 [30]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.25

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.02
upper limit	1.53

Notes:

[30] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Time to Start of Dopaminergic Parkinson's Disease Treatment

End point title	Time to Start of Dopaminergic Parkinson's Disease Treatment

End point description:

This endpoint is defined as the time between first dose of study medication and the date when the participant starts dopaminergic treatment. The median time to start of treatment would be the timepoint when more than 50% of all participants started the treatment. At the end of Week 52, less than 50% of the participants started the treatment, thus the median time to start of treatment was not estimable and is assigned a value of '99999999' in the results table.

End point type	Secondary

End point timeframe:

From baseline to Week 52

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	105	106	
Units: Days				
median (confidence interval 80%)	99999999 (99999999 to 99999999)	99999999 (99999999 to 99999999)	99999999 (99999999 to 99999999)	

Statistical analyses

Statistical analysis title	Low-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 Low Dose
Number of subjects included in analysis	210
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9542 [31]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.77
upper limit	1.33

Notes:

[31] - Nominal p-values are displayed for descriptive purposes only.

Statistical analysis title	High-Dose Group
Comparison groups	Part 1: Placebo v Part 1: RO7046015 High Dose
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4567 [32]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.63
upper limit	1.13

Notes:

[32] - Nominal p-values are displayed for descriptive purposes only.

Secondary: Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)

End point title	Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)

End point description:

An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An SAE was any AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly.

End point type	Secondary

End point timeframe:

From baseline to Week 52

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	105	106	
Units: Percentage of participants				
number (not applicable)				
AEs	82.9	93.3	91.5	
SAEs	4.8	6.7	7.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Drug Antibodies (ADAs) Against RO7046015

End point title	Percentage of Participants With Anti-Drug Antibodies (ADAs) Against RO7046015

End point description:

Samples of the participant's blood was taken to evaluate anti-drug antibodies (ADA). The number of ADA positive participants, Treatment-induced and Treatment-enhanced was reported. Treatment-induced = participants with ADA negative or missing data at baseline but develop an ADA response following exposure to the study drug. Treatment-enhanced = participants with ADA positive at baseline and the titre of one or more post-baseline samples is at least >=4 fold increase greater than the baseline titre sample.

End point type	Secondary

End point timeframe:

Baseline, Pre-dose (0 hours) on Weeks 4, 20, 36, 52, 56, 68, 80, and 104; at early termination (up to Week 104), and follow-up (12 weeks after last dose up to Week 116)

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[33]	104	105	
Units: Percentage of participants				
number (not applicable)		1.0	1.9	

Notes:

[33] - Only participants who received the study drug were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Clearance (CL) of RO7046015

End point title	Systemic Clearance (CL) of RO7046015

End point description:

Clearance is a measure of the rate at which a drug is removed from the body.

End point type	Secondary

End point timeframe:

Predose (0 hours) and end of infusion (infusion length=2 hours or less) on Baseline, Weeks 4, 20, 36, 52, 56, 68, 80, and 104; at Day 7, Day 14, early termination (up to Week 104), and follow-up (12 weeks after last dose up to Week 116)

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[34]	0[35]	0[36]	
Units: Micrograms per milliliter (ug/mL)				
median (confidence interval 90%)	(to)	(to)	(to)	

Notes:

[34] - Final results for this endpoint will be provided at the time of final results disclosure.

[35] - Final results for this endpoint will be provided at the time of final results disclosure.

[36] - Final results for this endpoint will be provided at the time of final results disclosure.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Volume of Distribution (Vz/F) of RO7046015

End point title	Apparent Volume of Distribution (Vz/F) of RO7046015
End point description:	
Volume of distribution is defined as the theoretical volume which the total amount of drug would need to be uniformly distributed to produce the desired plasma concentration of a drug.	
End point type	Secondary
End point timeframe:	
Predose (0 hours) and end of infusion (infusion length=2 hours or less) on Baseline, Weeks 4, 20, 36, 52, 56, 68, 80, and 104; at Day 7, Day 14, early termination (up to Week 104), and follow-up (12 weeks after last dose up to Week 116)	

End point values	Part 1: Placebo	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[37]	0[38]	0[39]	
Units: Micrograms per milliliter (ug/mL)				
median (confidence interval 90%)	(to)	(to)	(to)	

Notes:

[37] - Final results for this endpoint will be provided at the time of final results disclosure.

[38] - Final results for this endpoint will be provided at the time of final results disclosure.

[39] - Final results for this endpoint will be provided at the time of final results disclosure.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Serum Concentration-Time Curve (AUC) of RO7046015 over the Dosing Interval

End point title	Area Under the Serum Concentration-Time Curve (AUC) of RO7046015 over the Dosing Interval[40]
End point description:	
AUC is defined as the measure of RO7046015 plasma concentration over time.	
End point type	Secondary
End point timeframe:	
Baseline over the duration of the study	

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Participants in arms that received the study drug will be analyzed. At the time of these primary results, there is no data available. Final results for this endpoint will be provided at the time of

final results disclosure.

End point values	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[41]	0[42]		
Units: Micrograms per milliliter (ug.d/mL)				
median (confidence interval 90%)	(to)	(to)		

Notes:

[41] - Final results for this endpoint will be provided at the time of final results disclosure.

[42] - Final results for this endpoint will be provided at the time of final results disclosure.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of RO7046015 at Steady-state

End point title	Maximum Observed Serum Concentration (Cmax) of RO7046015 at Steady-state[43]

End point description:

Cmax is the maximum observed plasma concentration of RO7046015.

End point type	Secondary

End point timeframe:

Baseline over the duration of the study

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Participants in arms that received the study drug will be analyzed. At the time of these primary results, there is no data available. Final results for this endpoint will be provided at the time of final results disclosure.

End point values	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[44]	0[45]		
Units: Micrograms per milliliter (ug/mL)				
median (confidence interval 90%)	(to)	(to)		

Notes:

[44] - Final results for this endpoint will be provided at the time of final results disclosure.

[45] - Final results for this endpoint will be provided at the time of final results disclosure.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Ctrough) of RO7046015 at Steady-state

End point title	Minimum Observed Serum Concentration (Ctrough) of RO7046015 at Steady-state[46]

End point description:

Cmin is the minimum observed plasma concentration of RO7046015.

End point type	Secondary

End point timeframe:

Baseline over the duration of the study

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Participants in arms that received the study drug will be analyzed. At the time of these primary results, there is no data available. Final results for this endpoint will be provided at the time of final results disclosure.

End point values	Part 1: RO7046015 Low Dose	Part 1: RO7046015 High Dose		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[47]	0[48]		
Units: Micrograms per milliliter (ug/mL)				
median (confidence interval 90%)	(to)	(to)		

Notes:

[47] - Final results for this endpoint will be provided at the time of final results disclosure.

[48] - Final results for this endpoint will be provided at the time of final results disclosure.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 52

Adverse event reporting additional description:

AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.0.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Part 1: RO7046015 High Dose

Reporting group description:

Participants received RO7046015 at a high dose level (3500 mg for body weight <65 kilogram (kg) or 4500 mg for body weight >=65 kg) as an IV infusion Q4W up to 52 weeks in Part 1.

Reporting group title	Part 1: RO7046015 Low Dose

Reporting group description:

Participants received RO7046015 at a low dose level (1500 mg; for all body weights) as an IV infusion Q4W up to 52 weeks in Part 1.

Reporting group title	Part 1: Placebo

Reporting group description:

Participants received placebo as intravenous (IV) infusion every four weeks (Q4W) up to 52 weeks in Part 1.

Serious adverse events	Part 1: RO7046015 High Dose	Part 1: RO7046015 Low Dose	Part 1: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 106 (7.55%)	7 / 105 (6.67%)	5 / 105 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine benign neoplasm			
subjects affected / exposed	0 / 106 (0.00%)	0 / 105 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			

subjects affected / exposed	0 / 106 (0.00%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 106 (1.89%)	0 / 105 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	1 / 106 (0.94%)	0 / 105 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 105 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 105 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 106 (0.00%)	0 / 105 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 106 (0.00%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Parkinson's disease			
subjects affected / exposed	0 / 106 (0.00%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 106 (0.00%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 106 (0.00%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 105 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Behaviour disorder			
subjects affected / exposed	1 / 106 (0.94%)	0 / 105 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 106 (0.94%)	0 / 105 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 105 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			

	Part 1: RO7046015 High Dose	Part 1: RO7046015 Low Dose	Part 1: Placebo
subjects affected / exposed	1 / 106 (0.94%)	1 / 105 (0.95%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament disorder			
subjects affected / exposed	0 / 106 (0.00%)	0 / 105 (0.00%)	1 / 105 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 106 (0.94%)	0 / 105 (0.00%)	0 / 105 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Part 1: RO7046015 High Dose	Part 1: RO7046015 Low Dose	Part 1: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 106 (65.09%)	67 / 105 (63.81%)	57 / 105 (54.29%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	10 / 106 (9.43%)	5 / 105 (4.76%)	5 / 105 (4.76%)
occurrences (all)	15	9	7
Infusion related reaction			
subjects affected / exposed	35 / 106 (33.02%)	20 / 105 (19.05%)	17 / 105 (16.19%)
occurrences (all)	115	40	29
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 106 (11.32%)	10 / 105 (9.52%)	10 / 105 (9.52%)
occurrences (all)	15	19	12
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 106 (9.43%)	8 / 105 (7.62%)	6 / 105 (5.71%)
occurrences (all)	10	8	6
Nausea			

subjects affected / exposed	9 / 106 (8.49%)	5 / 105 (4.76%)	9 / 105 (8.57%)
occurrences (all)	16	6	10
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	3 / 106 (2.83%)	1 / 105 (0.95%)	6 / 105 (5.71%)
occurrences (all)	3	1	8
Psychiatric disorders			
Anxiety			
subjects affected / exposed	7 / 106 (6.60%)	2 / 105 (1.90%)	3 / 105 (2.86%)
occurrences (all)	7	2	3
Insomnia			
subjects affected / exposed	8 / 106 (7.55%)	3 / 105 (2.86%)	5 / 105 (4.76%)
occurrences (all)	9	3	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 106 (3.77%)	7 / 105 (6.67%)	8 / 105 (7.62%)
occurrences (all)	4	8	9
Back pain			
subjects affected / exposed	11 / 106 (10.38%)	8 / 105 (7.62%)	8 / 105 (7.62%)
occurrences (all)	13	8	9
Pain in extremity			
subjects affected / exposed	5 / 106 (4.72%)	6 / 105 (5.71%)	2 / 105 (1.90%)
occurrences (all)	6	7	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 106 (12.26%)	20 / 105 (19.05%)	15 / 105 (14.29%)
occurrences (all)	17	25	19
Upper respiratory tract infection			
subjects affected / exposed	9 / 106 (8.49%)	4 / 105 (3.81%)	9 / 105 (8.57%)
occurrences (all)	11	4	10

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 November 2017	The Safety and Efficacy Monitoring Committee was changed to a single independent Data Monitoring Committee; Sample size was adjusted; Immunogenicity population was corrected; Exclusion criteria was revised; Iodine pretreatment options were clarified; Enrollment criteria allowing participants on stable doses of a selective MAO-B inhibitor and SSRI or SNRI antidepressant was added; The number of study centres increased to help with recruitment; Revisions to the Schedule of Assessments.
27 June 2018	Exclusion criteria were clarified.
23 October 2019	Secondary objectives and endpoints were further specified and updated; Analysis population definitions were updated; Additional information on analyses was provided; Clarification of what constitutes a non-investigational medicinal product; Clarification of a medication error was added; Information regarding videotaping participants during administration of the MDS-UPDRS scale.
20 March 2020	Addition of Part 3 which is a 5-year all participants on treatment extension aiming to assess long-term safety and efficacy effects of RO7046015.

Notes:

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Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported