Clinical trial results:
A Double-blind, Placebo-controlled, Randomized, 18-month Phase 2a Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of Oral UCB0599 in Study Participants with Early Parkinson's Disease

Summary

EudraCT number	2020-003265-19
Trial protocol	DE FR PL ES NL IT
Global end of trial date	06 September 2024

Results information

Result version number	v2 (current)
This version publication date	16 November 2025
First version publication date	23 October 2025
Version creation reason	• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review.

Trial information

Trial identification

Sponsor protocol code	PD0053

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04658186
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
Public contact	UCB BIOSCIENCES GmbH, Clin Trial Reg & Results Disclosure, clinicaltrials@ucb.com
Scientific contact	UCB BIOSCIENCES GmbH, Clin Trial Reg & Results Disclosure, clinicaltrials@ucb.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	Final
Date of interim/final analysis	24 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 September 2024
Global end of trial reached?	Yes
Global end of trial date	06 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to demonstrate the superiority of UCB0599 over placebo with regard to clinical symptoms of disease progression over 12 and 18 months in participants diagnosed with early-stage Parkinson’s Disease (PD)

Protection of trial subjects:

During the conduct of the study all participants were closely monitored. DAT-SPECT related: Each study participant received a maximum of 3 injections of 123I-Ioflupane during the study, according to the approved label. The target single injection dose of 185MBq is estimated to result in a radiation burden of 4.63mSv and the total effective dose for the study will be 13.89mSv. This is categorized as a category III substantial risk level (ICR62), which is balanced by the substantial societal benefit from the results of this clinical study. A dose of a thyroid blocking agent was given before the radiotracer dose.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator: -

Actual start date of recruitment	30 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	France: 66
Country: Number of subjects enrolled	Germany: 58
Country: Number of subjects enrolled	Italy: 55
Country: Number of subjects enrolled	Netherlands: 22
Country: Number of subjects enrolled	Poland: 84
Country: Number of subjects enrolled	Spain: 28
Country: Number of subjects enrolled	United Kingdom: 32
Country: Number of subjects enrolled	United States: 130
Worldwide total number of subjects	496
EEA total number of subjects	313

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)	313
From 65 to 84 years	183
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in December 2020 and concluded in September 2024.

Pre-assignment

Screening details:

The Participant Flow refers to the Randomized Set.

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	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received UCB0599 matching-placebo capsules, orally, from Day 1 up to 18 months during treatment period.

Arm type	Placebo
Investigational medicinal product name	UCB0599 matching-placebo capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

UCB0599 matching-placebo capsules were administered orally, from Day 1 to Month 18

Arm title	UCB0599 180 mg/day

Arm description:

Participants received UCB0599 90 milligram (mg) capsules twice daily (BID), for a total daily dose of 180 mg, along with matching placebo capsules BID, administered orally from Day 1 up to 18 months during treatment period.

Arm type	Experimental
Investigational medicinal product name	UCB0599
Investigational medicinal product code	
Other name	Minzasolmin
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

UCB0599 180 mg/day capsules were administered orally, from Day 1 to Month 18.

Arm title	UCB0599 360 mg/day

Arm description:

Participants received UCB0599 180 mg capsules twice daily (BID), for a total daily dose of 360 mg, administered orally from Day 1 up to 18 months during treatment period.

Arm type	Experimental

Investigational medicinal product name	UCB0599
Investigational medicinal product code	
Other name	Minzasolmin
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

UCB0599 360 mg/day capsules were administered orally, from Day 1 to Month 18.

Number of subjects in period 1	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day
Started	165	166	165
Completed	154	138	139
Not completed	11	28	26
Participant is Moving in Another Province	-	1	-
Non-Compliance	-	1	1
Adverse event, non-fatal	4	18	15
Dropout on the Promotor's Decision	-	-	1
Worsening Symptoms; Participant Withdrew	-	-	1
Site Closure; Participant declined transfer	-	1	-
Lost to follow-up	-	-	2
Participant Not Eligible. Randomized In Error	1	-	1
Consent Withdrawn by Participant (not due to AE)	5	6	3
Lack of efficacy	1	1	-
Protocol deviation	-	-	1
PI Decision due to Participant Safety	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received UCB0599 matching-placebo capsules, orally, from Day 1 up to 18 months during treatment period.	
Reporting group title	UCB0599 180 mg/day
Reporting group description:	
Participants received UCB0599 90 milligram (mg) capsules twice daily (BID), for a total daily dose of 180 mg, along with matching placebo capsules BID, administered orally from Day 1 up to 18 months during treatment period.	
Reporting group title	UCB0599 360 mg/day
Reporting group description:	
Participants received UCB0599 180 mg capsules twice daily (BID), for a total daily dose of 360 mg, administered orally from Day 1 up to 18 months during treatment period.	

Reporting group values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day
Number of subjects	165	166	165
Age Categorical Units: participants			
18 years to less than (<) 65 years	98	105	110
65 years to <85 years	67	61	55
Age Continuous Units: years			
arithmetic mean	61.2	61.4	59.9
standard deviation	± 8.3	± 7.8	± 8.4
Sex: Female, Male Units: participants			
Female	65	66	65
Male	100	100	100

Reporting group values	Total		
Number of subjects	496		
Age Categorical Units: participants			
18 years to less than (<) 65 years	313		
65 years to <85 years	183		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: participants			
Female	196		
Male	300		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received UCB0599 matching-placebo capsules, orally, from Day 1 up to 18 months during treatment period.	
Reporting group title	UCB0599 180 mg/day
Reporting group description:	
Participants received UCB0599 90 milligram (mg) capsules twice daily (BID), for a total daily dose of 180 mg, along with matching placebo capsules BID, administered orally from Day 1 up to 18 months during treatment period.	
Reporting group title	UCB0599 360 mg/day
Reporting group description:	
Participants received UCB0599 180 mg capsules twice daily (BID), for a total daily dose of 360 mg, administered orally from Day 1 up to 18 months during treatment period.	

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Day 0

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Day 0[1]
End point description:	
MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. Full analysis set (FAS) included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.	
End point type	Primary
End point timeframe:	
Day 0	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	159	159	
Units: score on a scale				
arithmetic mean (standard deviation)	34.0 (± 13.2)	33.9 (± 16.4)	30.6 (± 13.4)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 2

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 2[2]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 2

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	156	144	
Units: score on a scale				
arithmetic mean (standard deviation)	34.7 (± 13.9)	34.8 (± 18.0)	30.3 (± 14.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 4

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 4[3]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 4

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	148	143	
Units: score on a scale				
arithmetic mean (standard deviation)	34.7 (± 14.9)	34.3 (± 18.6)	31.4 (± 15.0)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 6

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 6[4]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 6

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	154	147	146	
Units: score on a scale				
arithmetic mean (standard deviation)	37.9 (± 16.0)	36.6 (± 20.0)	32.9 (± 15.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 8

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 8[5]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 8

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	148	143	
Units: score on a scale				
arithmetic mean (standard deviation)	35.6 (± 14.3)	34.6 (± 19.7)	32.9 (± 15.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 10

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 10[6]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 10

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	141	140	
Units: score on a scale				
arithmetic mean (standard deviation)	35.6 (± 13.6)	33.7 (± 18.4)	33.2 (± 15.6)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 12

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 12[7]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 12

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	142	140	
Units: score on a scale				
arithmetic mean (standard deviation)	37.3 (± 15.3)	36.5 (± 19.2)	34.5 (± 15.4)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 14

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 14[8]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 14

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	154	137	141	
Units: score on a scale				
arithmetic mean (standard deviation)	37.1 (± 14.6)	34.8 (± 18.8)	33.9 (± 16.9)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 16

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 16[9]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 16

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	139	137	
Units: score on a scale				
arithmetic mean (standard deviation)	37.2 (± 15.6)	35.9 (± 19.8)	33.6 (± 15.4)	

Statistical analyses

No statistical analyses for this end point

Primary: Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 18

End point title	Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts I-III Sum Score at Month 18[10]

End point description:

MDS-UPDRS is multimodal scale. Part I assessed non-motor experiences of daily living and has 2 components (0–52 possible points). Part IA: 6 questions and assessed by examiner (0–24 possible points). Part IB: 7 questions on non-motor experiences of daily living completed (0–28 possible points). Part II assessed motor experiences of daily living (0–52 possible points) and includes 13 questions completed. Part III assessed motor signs of PD and was administered by rater (0–52 possible points). Part III: 33 questions based on 18 items. For all questions of each part, numeric score response options linked to accepted clinical terms: 0 to 4, 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. Total Score equals sum of Parts I, II, and III(Score: 0–236). Higher score = more severe PD symptoms. FAS included all randomized participants who received at least partial study dose and had >=1 post-Baseline assessment. Number analyzed includes those evaluable for this assessment.

End point type	Primary

End point timeframe:

Month 18

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	138	137	
Units: score on a scale				
arithmetic mean (standard deviation)	37.9 (± 15.5)	35.6 (± 18.1)	34.9 (± 16.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: MDS-UPDRS Part III Subscale

End point title	MDS-UPDRS Part III Subscale

End point description:

MDS-UPDRS part III includes motor items assessing speech, facial expression, rigidity, finger tapping, hand movements, pronation supination movements of hands, toe tapping, leg agility, arising from chair, gait, freezing of gait, postural stability, posture, global spontaneity of movement (body bradykinesia), postural tremor of the hands, kinetic tremor of the hands, rest tremor amplitude, and constancy of rest tremor. It included 33 scores based on 18-items, each anchored with 5 responses: 0=normal,1=slight,2=mild,3=moderate, 4=severe. The scale range was from 0 to 132, with a lower score = better motor function and a higher score = more severe motor symptoms. FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment. Here, "N" included all participants who were evaluable for this assessment and number analyzed (n) signifies participants who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Day 0, Months 2, 4, 6, 8, 10, 12, 14, 16, 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	162	164	
Units: score on a scale				
arithmetic mean (standard deviation)				
Day 0 (n=159, 162, 164)	22.6 (± 9.8)	21.9 (± 11.3)	20.4 (± 9.5)	
Month 2 (n=159, 158, 151)	22.9 (± 10.2)	22.7 (± 12.4)	20.0 (± 10.3)	
Month 4 (n= 157, 151, 147)	23.1 (± 10.5)	22.5 (± 12.7)	20.7 (± 10.6)	
Month 6 (n=157, 147, 147)	24.3 (± 10.9)	23.2 (± 12.4)	21.3 (± 10.8)	
Month 8 (n=156, 148, 145)	23.3 (± 10.0)	22.2 (± 12.6)	21.0 (± 10.7)	
Month 10 (n=156, 141, 140)	23.3 (± 9.2)	21.6 (± 12.1)	21.0 (± 11.0)	
Month 12 (n=153, 143, 140)	24.1 (± 10.0)	22.8 (± 12.0)	21.8 (± 10.5)	
Month 14 (n= 154, 139, 141)	24.1 (± 10.1)	22.2 (± 11.9)	21.8 (± 11.4)	
Month 16 (n=153, 139, 137)	24.3 (± 10.1)	22.8 (± 12.3)	21.7 (± 10.7)	
Month 18 (n=153, 138, 138)	24.2 (± 10.1)	23.0 (± 11.7)	22.2 (± 10.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: MDS-UPDRS Part III Early-stage Parkinson's Disease (ePD) Subscore on Selected Items

End point title	MDS-UPDRS Part III Early-stage Parkinson's Disease (ePD) Subscore on Selected Items

End point description:

The early-stage Parkinson's disease (ePD) subscore is derived from a 15-item subset of the MDS-UPDRS Part III (Motor Examination). It includes all rigidity assessments (neck, upper limbs [right/left], and lower limbs [right/left]) and bradykinesia-related tasks: finger tapping (right/left), hand movements (right/left), pronation-supination of hands (right/left), toe tapping (right/left), and leg agility (right/left). Each item is scored on a 5-point likert scale (0 = no problem to 4 = severe), resulting in a total ePD subscore range of 0 to 60. Higher scores indicate greater motor impairment, while lower scores reflect better motor function. FAS was used. "N"= all participants who were evaluable for this assessment; 'n'=participants who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Day 0, Months 2, 4, 6, 8, 10, 12, 14, 16, 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	162	164	
Units: score on a scale				
arithmetic mean (standard deviation)				
Day 0 (n= 159, 162, 164)	13.3 (± 7.11)	12.6 (± 7.96)	11.8 (± 6.85)	
Month 2 (n=159, 159, 151)	13.2 (± 7.33)	13.2 (± 8.48)	11.6 (± 7.57)	
Month 4 (n=157, 151, 147)	13.4 (± 7.50)	13.1 (± 8.76)	11.8 (± 7.64)	
Month 6 (157, 148, 147)	13.9 (± 7.39)	13.4 (± 8.42)	12.4 (± 7.58)	
Month 8 (157, 148, 146)	13.4 (± 6.82)	12.7 (± 8.60)	11.8 (± 7.49)	
Month 10 (n=156, 141, 141)	13.4 (± 6.46)	12.1 (± 8.14)	11.9 (± 7.98)	
Month 12 (n=153, 144, 142)	13.7 (± 6.98)	12.7 (± 8.20)	12.9 (± 7.61)	
Month 14 (n=154, 142, 141)	13.8 (± 7.14)	12.7 (± 8.35)	12.5 (± 7.88)	
Month 16 (n=153, 139, 138)	13.8 (± 7.24)	12.9 (± 8.26)	12.4 (± 7.83)	
Month 18 (n=153, 138, 138)	13.8 (± 7.34)	12.9 (± 7.90)	12.6 (± 7.61)	

Statistical analyses

No statistical analyses for this end point

Secondary: MDS-UPDRS Part II Subscale

End point title	MDS-UPDRS Part II Subscale

End point description:

MDS-UPDRS part II includes motor items assessing speech, saliva and drooling, chewing and swallowing, eating tasks (cutting food and handling utensils), dressing, hygiene, handwriting, doing hobbies and other activities, turning in bed, tremor, getting out of bed, a car or a deep chair, walking and balance, and freezing. Each of the items in the UPDRS is measured on a scale. It included 13-items, each anchored with 5 responses: 0 = normal, 1 = slight, 2 = mild, 3 = moderate, and 4 = severe. The scale range for Part II was 0-52, with higher scores reflecting greater severity. FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment. Here, number of participants analyzed included all participants who were evaluable for this assessment and 'n' signifies participants who were evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Day 0, Months 2, 4, 6, 8, 10, 12, 14, 16, 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	163	161	
Units: score on a scale				
arithmetic mean (standard deviation)				
Day 0 (n=163, 163, 161)	6.0 (± 4.0)	6.3 (± 4.6)	5.7 (± 4.3)	
Month 2 (n=158, 160, 149)	6.5 (± 4.3)	6.9 (± 5.2)	6.1 (± 4.1)	
Month 4 (156, 150, 147)	6.8 (± 4.6)	7.1 (± 5.4)	6.4 (± 4.5)	
Month 6 (n=156, 148, 147)	7.7 (± 5.1)	7.7 (± 6.2)	6.7 (± 5.0)	
Month 8 (n=158, 148, 145)	7.0 (± 4.6)	7.1 (± 5.7)	6.9 (± 4.7)	
Month 10 (n=156, 142, 143)	6.9 (± 4.5)	6.7 (± 5.4)	7.1 (± 4.7)	
Month 12 (153, 144, 143)	6.9 (± 4.9)	7.3 (± 5.5)	7.3 (± 5.1)	
Month 14 (n=154, 140, 142)	7.1 (± 4.8)	7.2 (± 5.8)	7.0 (± 5.1)	
Month 16 (152, 140, 138)	7.1 (± 5.1)	7.2 (± 5.7)	6.7 (± 4.5)	
Month 18 (n=152, 138, 138)	7.3 (± 5.0)	6.8 (± 5.2)	7.3 (± 5.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: MDS-UPDRS Part I Subscale

End point title	MDS-UPDRS Part I Subscale

End point description:

MDS-UPDRS PartI includes several non-motor aspects of experiences of daily living including cognitive impairment,hallucinations and psychosis,depressed mood,anxious mood,apathy,features of dopamine dysregulation syndrome during Part IA;and sleep problems,daytime sleepiness,pain and other sensation,urinary problems,constipation problems,light headedness on standing, and fatigue during PartIB. PartI assessed non-motor experiences of daily living, has 2 components ranging:0–52.PartIA contained 6questions and assessed by examiner ranging:0–24. PartIB contained 7questions on non-motor experiences of daily living and completed by participant ranging:0–28. Each item measured on scale of 0 to 4, 0=normal and 4=severe abnormalities/worse outcome. Total Score Range 0 to 52, which is sum of Part IA(0-24) and Part IB(0-28) subscale scores. Higher scores=greater severity of non-motor symptoms. FAS. "N"=participants evaluable for assessment and 'n'=participants evaluable at specified timepoints.

End point type	Secondary

End point timeframe:

Day 0, Months 2, 4, 6, 8, 10, 12, 14, 16, 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	158	161	158	
Units: score on a scale				
arithmetic mean (standard deviation)				
Day 0 (n= 158, 161, 158)	5.4 (± 3.9)	5.5 (± 4.4)	4.7 (± 3.7)	
Month 2 (n= 155, 160, 145)	5.2 (± 4.2)	5.2 (± 3.8)	4.3 (± 3.5)	
Month 4 (n=153, 149, 144)	5.1 (± 4.4)	5.0 (± 4.0)	4.5 (± 3.8)	
Month 6 (n=154, 148, 146)	5.9 (± 4.8)	5.7 (± 4.5)	5.1 (± 3.9)	
Month 8 (n=156, 148, 147)	5.5 (± 4.4)	5.3 (± 4.2)	5.0 (± 3.9)	

Month 10 (n=156, 142, 143)	5.4 (± 4.2)	5.4 (± 4.1)	4.9 (± 4.1)	
Month 12 (n=152, 143, 143)	6.2 (± 5.1)	6.2 (± 4.8)	5.3 (± 4.4)	
Month 14 (n=154, 141, 142)	5.9 (± 4.6)	5.8 (± 5.0)	5.0 (± 4.2)	
Month 16 (n= 153, 140, 138)	5.9 (± 4.8)	5.9 (± 5.1)	5.1 (± 4.1)	
Month 18 (n=152, 138, 138)	6.4 (± 5.1)	5.9 (± 4.6)	5.3 (± 4.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Emerging Symptoms in Participants as Measured by MDS-UPDRS Part II

End point title	Emerging Symptoms in Participants as Measured by MDS-UPDRS Part II

End point description:

The participant was considered to have an emerging symptom for the item, if the change from Baseline for the item is greater than 0 for 2 consecutive visits. The magnitude of change from Baseline was not considered to determine the emerging symptom. Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part II includes motor items assessing speech, saliva and drooling, chewing and swallowing, eating tasks (cutting food and handling utensils), dressing, hygiene, handwriting, doing hobbies and other activities, turning in bed, tremor, getting out of bed, a car or a deep chair, walking and balance, and freezing. This included 13-items, each anchored with 5 responses: 0 = normal, 1 = slight, 2 = mild, 3 = moderate, and 4 = severe. The scale range for Part II was 0-52, with higher scores = greater severity. FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment.

End point type	Secondary

End point timeframe:

Baseline to Month 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	164	164	
Units: participants				
Number of Emerging symptoms: 0	28	36	38	
Number of Emerging symptoms: 1	18	41	31	
Number of Emerging symptoms: 2	35	33	23	
Number of Emerging symptoms: 3	37	15	26	
Number of Emerging symptoms: 4	15	13	15	
Number of Emerging symptoms: 5	15	13	14	
Number of Emerging symptoms: 6	4	7	10	
Number of Emerging symptoms: 7	4	4	4	
Number of Emerging symptoms: 8	4	1	3	
Number of Emerging symptoms: 9	2	1	0	
Number of Emerging symptoms: 10	1	0	0	
Number of Emerging symptoms: 11	0	0	0	
Number of Emerging symptoms: 12	0	0	0	
Number of Emerging symptoms: 13	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Worsening of the Disease as Measured by MDS-UPDRS Part III

End point title	Time to Worsening of the Disease as Measured by MDS-UPDRS Part III

End point description:

Time to worsening of the disease on the MDS-UPDRS III scale as defined by a 5-point increase in MDS-UPDRS III, within the 18-month period. MDS-UPDRS part III includes motor items assessing speech,facial expression,rigidity,finger tapping,hand movements,pronation supination movements of hands,toe tapping,leg agility,arising from chair,gait,freezing of gait,postural stability,posture,global spontaneity of movement (body bradykinesia), postural tremor of hands,kinetic tremor of hands,rest tremor amplitude, and constancy of rest tremor. It included 33 scores based on 18-items, each anchored with 5 responses: 0=normal,1=slight,2=mild,3=moderate, 4=severe. Scale ranges: 0-132, with lower score = better motor function; higher score = more severe motor symptoms. FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment.

End point type	Secondary

End point timeframe:

Baseline to Month 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	164	164	
Units: months				
arithmetic mean (confidence interval 95%)	8.64 (7.7236 to 9.5635)	8.95 (7.8974 to 10.0012)	9.45 (8.4743 to 10.4340)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Results obtained from generalized linear model for RMET, with gender and age at baseline as covariates and treatment group as effect of interest.

Comparison groups	Placebo v UCB0599 360 mg/day
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.214
Method	Wald Chi-square
Parameter estimate	Difference in RMET
Point estimate	0.81

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	2.09

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Results were obtained from a generalized linear model for the restricted mean event time (RMET), with gender and age at baseline as covariates and treatment group as the effect of interest.

Comparison groups	Placebo v UCB0599 180 mg/day
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.647
Method	Wald Chi-square
Parameter estimate	Difference in RMET
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.61

Secondary: Montreal Cognitive Assessment (MoCA)

End point title	Montreal Cognitive Assessment (MoCA)

End point description:

The Montreal Cognitive Assessment (MoCA) is a standardized screening tool used to evaluate mild cognitive impairment across multiple cognitive functions i.e. visuospatial/executive function, naming, memory, attention, language, abstraction, delayed recall, and orientation. The total possible score is calculated by summing the scores across all functions ranges from: 0 to 30. A score of 26 or above is considered normal, a lower score indicates cognitive impairment. FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment. Here, 'n' signifies participants who were evaluable at each specified timepoints.

End point type	Secondary

End point timeframe:

Screening, Month 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	164	164	
Units: score on a scale				
arithmetic mean (standard deviation)				
Screening (n=163, 164, 164)	27.8 (± 1.8)	27.6 (± 2.0)	27.8 (± 1.7)	
Month 18 (n= 152, 137, 136)	27.4 (± 2.2)	27.3 (± 2.4)	27.3 (± 2.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Screening in Dopamine Transporter Imaging with Single Photon Emission Computed Tomography (DaT-SPECT) Mean Striatum Specific Binding Ratios (SBR)

End point title	Change from Screening in Dopamine Transporter Imaging with Single Photon Emission Computed Tomography (DaT-SPECT) Mean Striatum Specific Binding Ratios (SBR)

End point description:

The change from screening in mean striatum specific binding ratios (SBR) was assessed by DaT-SPECT using 123I-Ioflupane as radiopharmaceutical. The whole striatum was calculated as the average of the SBR data values for the four following "small" regions: left caudate small, left putamen small, right caudate small and right putamen small. The SBR was calculated for each region with the occipital cortex as a reference region, where a lower SBR indicates worse disease. The following formula was used to calculate this: (Average [Small region] – Average [Occipital region])/ (Average [Occipital region]). FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment. Here, number of participants analyzed included all participants who were evaluable for this assessment and 'n' signifies participants who were evaluable at each specified timepoints.

End point type	Secondary

End point timeframe:

Screening, Months 12 and 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	133	130	
Units: specific binding ratio				
arithmetic mean (standard deviation)				
Whole striatum:Month (M) 12(n=133,130,111)	-0.202 (± 0.215)	-0.141 (± 0.194)	-0.102 (± 0.254)	
Whole striatum: M18 (n=140,124,130)	-0.233 (± 0.226)	-0.182 (± 0.232)	-0.193 (± 0.254)	
Ipsilateral striatum: M 12 (n=114,114,95)	-0.237 (± 0.262)	-0.161 (± 0.246)	-0.093 (± 0.294)	
Ipsilateral striatum: M 18 (n=123,109,114)	-0.260 (± 0.263)	-0.211 (± 0.282)	-0.194 (± 0.318)	
Contralateral striatum: M 12 (n=114,114,95)	-0.161 (± 0.210)	-0.138 (± 0.209)	-0.099 (± 0.278)	
Contralateral striatum: M 18 (n=123,109,114)	-0.203 (± 0.214)	-0.169 (± 0.237)	-0.188 (± 0.259)	
Ipsilateral caudate small: M 12 (n=114,114,95)	-0.296 (± 0.380)	-0.196 (± 0.352)	-0.080 (± 0.485)	
Ipsilateral caudate small: M 18 (n=123,109,114)	-0.312 (± 0.383)	-0.273 (± 0.390)	-0.210 (± 0.439)	
Ipsilateral putamen small: M 12 (n=114,114,95)	-0.178 (± 0.260)	-0.125 (± 0.255)	-0.106 (± 0.219)	

Ipsilateral putamen small: M 18 (n=123,109,114)	-0.208 (± 0.252)	-0.150 (± 0.260)	-0.179 (± 0.270)	
Contralateral caudate small: M 12 (n=114,114,95)	-0.256 (± 0.328)	-0.183 (± 0.332)	-0.145 (± 0.363)	
Contralateral caudate small: M 18 (n=123,109,114)	-0.291 (± 0.330)	-0.263 (± 0.370)	-0.248 (± 0.398)	
Contralateral putamen small: M 12 (114,114,95)	-0.066 (± 0.190)	-0.094 (± 0.223)	-0.053 (± 0.304)	
Contralateral putamen small: M 18 (n=123,109,114)	-0.115 (± 0.190)	-0.076 (± 0.197)	-0.128 (± 0.209)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Start of Symptomatic Treatment (ST)

End point title	Time to Start of Symptomatic Treatment (ST)

End point description:

Time to start of symptomatic treatment (ST) within the 18-month period. FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment.

End point type	Secondary

End point timeframe:

Baseline to Month 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	163	164	164	
Units: months				
arithmetic mean (confidence interval 95%)	10.58 (9.6242 to 11.5456)	11.59 (10.6084 to 12.5623)	11.80 (10.8312 to 12.7735)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Results were obtained from a generalized linear model for the RMET, with gender and age at baseline as covariates and treatment group as the effect of interest.

Comparison groups	Placebo v UCB0599 180 mg/day

Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.124
Method	Wald Chi-square
Parameter estimate	Difference in RMET
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	2.27

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Results were obtained from a generalized linear model for the RMET, with gender and age at baseline as covariates and treatment group as the effect of interest.

Comparison groups	Placebo v UCB0599 360 mg/day
Number of subjects included in analysis	327
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064
Method	Wald Chi-sqaure
Parameter estimate	Difference in RMET
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	2.51

Secondary: Symptomatic Treatment (ST) Intake

End point title	Symptomatic Treatment (ST) Intake

End point description:

Cumulative number of participants on symptomatic treatment (ST) at 18 months are reported. FAS included all randomized study participants who received at least a partial dose of study medication, have at least 1 post-Baseline assessment. Here, number of participants analyzed included all participants who were evaluable for this assessment.

End point type	Secondary

End point timeframe:

Month 18

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	153	139	140	
Units: participants	111	89	88	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment-emergent Adverse Events (TEAEs)

End point title	Percentage of Participants With Treatment-emergent Adverse Events (TEAEs)

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study medication, whether or not considered related to the study medication. A TEAE is defined as any AE with a start date on or after the first dose of treatment or any unresolved event already present before administration of treatment that worsens in intensity following exposure to the treatment. Safety set included all randomized study participants who receive at least a partial dose of study medication.

End point type	Secondary

End point timeframe:

From Baseline up to 30 days of safety follow-up after the last dose of the study drug (up to 19 months)

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	165	164	
Units: percentage of participants				
number (not applicable)	87.8	86.7	87.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Serious TEAEs

End point title	Percentage of Participants With Serious TEAEs

End point description:

Serious adverse event: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Safety set included all randomized study participants who receive at least a partial dose of study medication.

End point type	Secondary

End point timeframe:

From Baseline up to 30 days of safety follow-up after the last dose of the study drug (up to 19 months)

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	165	164	
Units: percentage of participants				
number (not applicable)	5.5	7.9	8.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With TEAEs Leading to Participant Withdrawal

End point title	Percentage of Participants With TEAEs Leading to Participant Withdrawal

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study medication, whether or not considered related to the study medication. A TEAE is defined as any AE with a start date on or after the first dose of treatment or any unresolved event already present before administration of treatment that worsens in intensity following exposure to the treatment. Safety set included all randomized study participants who receive at least a partial dose of study medication.

End point type	Secondary

End point timeframe:

From Baseline up to 30 days of safety follow-up after the last dose of the study drug (up to 19 months)

End point values	Placebo	UCB0599 180 mg/day	UCB0599 360 mg/day	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	164	165	164	
Units: percentage of participants				
number (not applicable)	2.4	10.9	9.8	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to 30 days of safety follow-up after the last dose of the study drug (up to 19 months)

Adverse event reporting additional description:

Safety analysis set included all randomized study participants who received at least a partial dose of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received UCB0599 matching-placebo capsules, orally, (4 UCB0599 matching-placebo capsules) twice per day (BID) from Day 1 up to 18 months.

Reporting group title	UCB0599 360 mg/day

Reporting group description:

Participants received UCB0599 180 mg capsules twice daily (BID), for a total daily dose of 360 mg, administered orally from Day 1 up to 18 months during treatment period.

Reporting group title	UCB0599 180 mg/day

Reporting group description:

Participants received UCB0599 90 milligram (mg) capsules twice daily (BID), for a total daily dose of 180 mg, along with matching placebo capsules BID, administered orally from Day 1 up to 18 months during treatment period.

Serious adverse events	Placebo	UCB0599 360 mg/day	UCB0599 180 mg/day
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 164 (5.49%)	14 / 164 (8.54%)	13 / 165 (7.88%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events	0	1	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Metastatic gastric cancer			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Prostate cancer			

subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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
Malignant melanoma			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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			
Fall			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative ileus			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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

Acute coronary syndrome			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Mitral valve prolapse			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	2 / 164 (1.22%)	0 / 164 (0.00%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord paralysis			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal polyp			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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
Diarrhoea			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Inguinal hernia			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Hepatobiliary disorders			
Hepatic cytolysis			

subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Erythema			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Rash			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Acute kidney injury			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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

Urinary bladder polyp			
subjects affected / exposed	0 / 164 (0.00%)	0 / 164 (0.00%)	1 / 165 (0.61%)
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			
Diverticulitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Coronavirus infection			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Pneumonia			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Infectious pleural effusion			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 164 (0.00%)	1 / 164 (0.61%)	0 / 165 (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
Urosepsis			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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
Urinary tract infection			
subjects affected / exposed	1 / 164 (0.61%)	0 / 164 (0.00%)	0 / 165 (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	Placebo	UCB0599 360 mg/day	UCB0599 180 mg/day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 164 (62.20%)	89 / 164 (54.27%)	97 / 165 (58.79%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	9 / 164 (5.49%)	12 / 164 (7.32%)	17 / 165 (10.30%)
occurrences (all)	9	14	22
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 164 (9.76%)	16 / 164 (9.76%)	11 / 165 (6.67%)
occurrences (all)	17	24	25
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 164 (7.32%)	7 / 164 (4.27%)	13 / 165 (7.88%)
occurrences (all)	14	7	15
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 164 (4.88%)	8 / 164 (4.88%)	12 / 165 (7.27%)
occurrences (all)	15	8	14
Diarrhoea			
subjects affected / exposed	8 / 164 (4.88%)	9 / 164 (5.49%)	10 / 165 (6.06%)
occurrences (all)	10	10	18
Constipation			
subjects affected / exposed	14 / 164 (8.54%)	8 / 164 (4.88%)	7 / 165 (4.24%)
occurrences (all)	14	9	7
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	9 / 164 (5.49%)	11 / 164 (6.71%)	5 / 165 (3.03%)
occurrences (all)	10	11	5
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	17 / 164 (10.37%)	12 / 164 (7.32%)	15 / 165 (9.09%)
occurrences (all)	17	14	19
Arthralgia			

subjects affected / exposed	19 / 164 (11.59%)	4 / 164 (2.44%)	14 / 165 (8.48%)
occurrences (all)	22	4	14
Infections and infestations			
COVID-19			
subjects affected / exposed	35 / 164 (21.34%)	32 / 164 (19.51%)	22 / 165 (13.33%)
occurrences (all)	38	33	23
Urinary tract infection			
subjects affected / exposed	15 / 164 (9.15%)	12 / 164 (7.32%)	18 / 165 (10.91%)
occurrences (all)	20	14	26
Nasopharyngitis			
subjects affected / exposed	19 / 164 (11.59%)	14 / 164 (8.54%)	14 / 165 (8.48%)
occurrences (all)	20	15	16
Influenza			
subjects affected / exposed	10 / 164 (6.10%)	14 / 164 (8.54%)	6 / 165 (3.64%)
occurrences (all)	10	15	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 October 2020	Protocol Amendment 1 was dated 29 Oct 2020. The purpose of this substantial amendment was to remove planned video recording of participants during the MDS-UPDRS Part III assessment due to operational limitations (example, procedures for de-identification, video processing, video data handling, access, and storage).
21 May 2021	Protocol Amendment 2 was dated 21 May 2021. The purpose of this substantial amendment was to increase the upper age limit for participants' inclusion in the study to 75 years, to reflect the ePD population. This population did not present additional risk compared to the population initially included in the study.
04 October 2021	Protocol Amendment 3 was dated 04 Oct 2021. The purpose of this substantial amendment was to add a treatment group with a lower dose of UCB0599, allowed the use of historical symptomatic treatments, and harmonized feedback from regulatory authorities and ethic review boards received during the initial Clinical Trial Applications.
24 February 2022	Protocol Amendment 4 was dated 24 Feb 2022. The purpose of this substantial amendment was to amend exclusion and discontinuation criteria regarding renal function, diabetes, and electrocardiograph (ECG) abnormalities to better reflect the parameters in the targeted study population.
30 June 2023	Protocol Amendment 5 was dated 30 Jun 2023. The purpose of this substantial amendment was to incorporate additional laboratory tests at Day 150 in order to allow for close monitoring of liver function test parameters.
21 March 2024	Protocol Amendment 6 was dated 21 Mar 2024. The purpose of this substantial amendment was to provided clarification around blinding and the timing of the Month 12 data analysis, and remove analyses that were no longer needed. In addition, the list of secondary and exploratory efficacy endpoints was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported