



Clinical trial results:

A Phase 2, Multicenter, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of AL001 in Heterozygous Carriers of Granulin or C9orf72 Mutations Causative of Frontotemporal Dementia

Summary

EudraCT number	2019-000138-20
Trial protocol	GB DE NL IT
Global end of trial date	05 June 2024

Results information

Result version number	v1 (current)
This version publication date	16 May 2025
First version publication date	16 May 2025

Trial information

Trial identification

Sponsor protocol code	AL001-2
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03987295
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alector Inc.
Sponsor organisation address	131 Oyster Point Boulevard, Suite 600, South San Francisco, United States, CA 94080
Public contact	Alector Medical Information, Alector Inc., +1 650-826-2454, medinfo@alektor.com
Scientific contact	Alector Medical Information, Alector Inc., +1 650-826-2454, medinfo@alektor.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	10 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2024
Global end of trial reached?	Yes
Global end of trial date	05 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part 1: To evaluate the safety and tolerability of intravenous (IV) administration of latozinemab over 96 weeks in asymptomatic and symptomatic carriers of a granulin (GRN) mutation causative of frontotemporal dementia (FTD) and in symptomatic carriers of a C9orf72 mutation causative of FTD.

Part 2: To assess the long-term safety and tolerability of latozinemab in participants who have completed 96 weeks of treatment on Part 1 of the study.

Protection of trial subjects:

This trial was designed and monitored in accordance with Alector procedures, which comply with the ethical principles of Good Clinical Practice (GCP) and the International Council for Harmonisation (ICH) as required by the major regulatory authorities, and in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy:

The most common concomitant medications were: psycholeptics, psychoanaleptics, lipid modifying agents, and vaccines (including influenza and COVID-19).

Evidence for comparator:

This was an open-label study.

Actual start date of recruitment	27 September 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	United States: 15
Country: Number of subjects enrolled	Canada: 5
Worldwide total number of subjects	33
EEA total number of subjects	10

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)	23
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 45 participants enrolled of which 33 received at least one dose of AL001-2 in Part 1; 12 of these participants had rolled over from Phase 1 study AL001-1. 16 participants completed Part 1 - 3 did not enroll in Part 2 and were counted as completed study, and 13 enrolled in Part 2. 9 participants completed both Part 1 and Part 2.

Pre-assignment

Screening details:

Part 1: Screening within 6 weeks prior to Day 1

Period 1

Period 1 title	Part 1 + Part 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Part 1 was 96-week evaluation of safety, tolerability, PK, PD and clinical effect of latozinemab administered intravenously (60 mg/kg, every 4 weeks [q4w]) for a total of 25 doses (96-week dosing period). Part 2 was for eligible participants who had completed the 96-week Part 1 treatment period. The OLE period evaluated the long-term safety and tolerability of latozinemab administered at the same dose and regimen as Part 1 (60 mg/kg, q4w) for up to a total of 25 doses (96-week optional OLE period)

Arms

Are arms mutually exclusive?	Yes
Arm title	aFTD-GRN

Arm description:

aFTD-GRN - asymptomatic frontotemporal dementia with heterozygous progranulin gene mutation

Arm type	Experimental
Investigational medicinal product name	AL001
Investigational medicinal product code	
Other name	Latozinemab (human recombinant anti-human Sortilin IgG1 monoclonal antibody)
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Part 1 - Latozinemab administered intravenously (60 mg/kg, every 4 weeks [q4w]), for a total of 25 doses (96-week dosing period);

Part 2 - Latozinemab administered intravenously (60 mg/kg, every 4 weeks [q4w]), for a total of 25 doses (96-week dosing period).

Arm title	FTD-GRN
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Arm description:

FTD-GRN - symptomatic carriers of GRN mutation causative of FTD

Arm type	Experimental
Investigational medicinal product name	AL001
Investigational medicinal product code	
Other name	Latozinemab (human recombinant anti-human Sortilin IgG1 monoclonal antibody)
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Part 1 - Latozinemab administered intravenously (60 mg/kg, every 4 weeks [q4w]), for a total of 25

doses (96-week dosing period);
Part 2 - Latozinemab administered intravenously (60 mg/kg, every 4 weeks [q4w]), for a total of 25 doses (96-week dosing period).

Arm title	FTD-C9orf72
Arm description: FTD-C9orf72 - symptomatic carriers of C9orf72 hexanucleotide repeat expansion mutation causative of FTD	
Arm type	Experimental
Investigational medicinal product name	AL001
Investigational medicinal product code	
Other name	Latozinemab (human recombinant anti-human Sortilin IgG1 monoclonal antibody)
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Part 1 - Latozinemab administered intravenously (60 mg/kg, every 4 weeks [q4w]), for a total of 25 doses (96-week dosing period);

Part 2 - Latozinemab administered intravenously (60 mg/kg, every 4 weeks [q4w]), for a total of 25 doses (96-week dosing period).

Number of subjects in period 1	aFTD-GRN	FTD-GRN	FTD-C9orf72
Started	5	12	16
Completed	5	5	6
Not completed	0	7	10
Administrative or Other Reasons	-	2	2
Withdrawal by Participant	-	4	6
Death	-	-	1
Investigator Discretion	-	1	-
Long-Term care facility placement and requires con	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	aFTD-GRN
Reporting group description: aFTD-GRN - asymptomatic frontotemporal dementia with heterozygous progranulin gene mutation	
Reporting group title	FTD-GRN
Reporting group description: FTD-GRN - symptomatic carriers of GRN mutation causative of FTD	
Reporting group title	FTD-C9orf72
Reporting group description: FTD-C9orf72 - symptomatic carriers of C9orf72 hexanucleotide repeat expansion mutation causative of FTD	

Reporting group values	aFTD-GRN	FTD-GRN	FTD-C9orf72
Number of subjects	5	12	16
Age categorical Units: Subjects			
Adults (18-64 years)	5	7	11
From 65-84 years	0	5	5
Age continuous Units: years			
median	59.0	59.5	60.0
full range (min-max)	32 to 63	48 to 78	40 to 74
Gender categorical Units: Subjects			
Female	1	4	9
Male	4	8	7

Reporting group values	Total		
Number of subjects	33		
Age categorical Units: Subjects			
Adults (18-64 years)	23		
From 65-84 years	10		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	14		
Male	19		

End points

End points reporting groups

Reporting group title	aFTD-GRN
Reporting group description: aFTD-GRN - asymptomatic frontotemporal dementia with heterozygous progranulin gene mutation	
Reporting group title	FTD-GRN
Reporting group description: FTD-GRN - symptomatic carriers of GRN mutation causative of FTD	
Reporting group title	FTD-C9orf72
Reporting group description: FTD-C9orf72 - symptomatic carriers of C9orf72 hexanucleotide repeat expansion mutation causative of FTD	

Primary: Duration of exposure to study drug (days)

End point title	Duration of exposure to study drug (days) ^[1]
End point description: The median exposure was 700 days (23 months) for the whole Safety Population. The median exposure was 1406 days (46 months) in the aFTD-GRN cohort, 498 days (16 months) in the FTD-GRN cohort, and 675 (22 months) days in the FTD-C9orf72 cohort.	
End point type	Primary
End point timeframe: Part 1 - 96 weeks + Part 2 - 96 weeks	

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: There is no statistical analysis for this primary end point.

End point values	aFTD-GRN	FTD-GRN	FTD-C9orf72	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	12	16	
Units: day				
median (full range (min-max))				
Duration of exposure to study drug (days)	1406.0 (1398 to 1407)	498.0 (111 to 1395)	675.0 (28 to 1407)	

Statistical analyses

No statistical analyses for this end point

Primary: Severity of TEAEs

End point title	Severity of TEAEs ^[2]
End point description: In total, 31 out of 33 (93.9%) participants experienced a TEAE of which 75.8% had mild or moderate TEAEs in severity; no treatment-related TEAEs were considered severe (or worse) in severity. There were no treatment-related TEAEs observed in the study and of the 6 TEAEs, one was fatal.	
End point type	Primary

End point timeframe:

Part 1 - 96 weeks + Part 2 - 96 weeks

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: There is no statistical analysis for this primary end point.

End point values	aFTD-GRN	FTD-GRN	FTD-C9orf72	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	12	16	
Units: Event				
number (not applicable)				
Mild	43	58	84	
Moderate	4	9	24	
Severe	3	1	4	
Life Threatening	0	0	0	
Death	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Severity of Treatment-Related TEAEs

End point title	Severity of Treatment-Related TEAEs ^[3]
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End point description:

End point type	Primary
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End point timeframe:

Part 1 - 96 weeks + Part 2 - 96 weeks

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: There is no statistical analysis for this primary end point.

End point values	aFTD-GRN	FTD-GRN	FTD-C9orf72	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	12	16	
Units: Event				
number (not applicable)				
Mild	5	1	12	
Moderate	1	1	5	
Severe	0	0	0	
Life Threatening	0	0	0	
Death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Any TEAE Leading to Study Drug Discontinuation

End point title Any TEAE Leading to Study Drug Discontinuation^[4]

End point description:

Two TEAEs led to latozinemab discontinuation. One participant in the FTD-GRN cohort with a medical history of mitral valve prolapse and incompetence had worsening that led to a valvuloplasty procedure and withdrawal from the study. One participant in the FTD-C9orf72 cohort experienced progression of ALS and was admitted to hospice, discontinuing the study.

End point type Primary

End point timeframe:

Part 1 - 96 weeks + Part 2 - 96 weeks

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: There is no statistical analysis for this primary end point.

End point values	aFTD-GRN	FTD-GRN	FTD-C9orf72	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	12	16	
Units: Event				
number (not applicable)				
Any TEAE Leading to Study Drug Discontinuation	0	1	1	

Statistical analyses

No statistical analyses for this end point

Primary: Immunogenicity Antidrug Antibodies (ADA)

End point title Immunogenicity Antidrug Antibodies (ADA)^[5]

End point description:

Across all cohorts, the ADA positivity rate ranged from 3% (3/33) to 33% (11/33) across dosing visits. In aFTD-GRN cohort, 3 out of 5 (60%) participants had ADA 2 weeks after the first dose. In FTD-GRN cohort, 3 out of 12 (25.0%) participants had ADA 2 weeks after the first dose; in FTD-C9orf72 cohort, 3 out of 16 (18.8%) participants had ADA 2 weeks after the first dose. Only 1 out of 33 (3%) participants was ADA positive before the 2nd dose administration. After multiple dose administration, the highest ADA positivity rate, 24.2% (8/33), was found at Week 13 after every 4 weeks of administration. After 52 weeks of treatment with latozinemab, only 2 out of 33 (6.1%) participants were ADA-positive across all cohorts. Median (min-max) ADA titer was 40 (20-5120) at 2 weeks after the first dose and was 240 (160-320) at Week 52. The higher incidence of ADA 2 weeks after the first dose could be probably due to the fact that 12 of these participants had rolled over from Phase 1 study AL001-1.

End point type Primary

End point timeframe:

Part 1 - 96 weeks + Part 2 - 96 weeks

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: There is no statistical analysis for this primary end point.

End point values	aFTD-GRN	FTD-GRN	FTD-C9orf72	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	12	16	
Units: percent				
median (full range (min-max))				
Week 2 - ADA Titer	320.0 (20 to 5120)	20.0 (20 to 2560)	40.0 (20 to 160)	
Week 13 - ADA Titer	160.0 (20 to 2560)	160.0 (160 to 640)	120.0 (80 to 160)	
Week 53 - ADA Titer	0 (0 to 0)	320.0 (320 to 320)	160.0 (160 to 160)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Latozinemab has an acceptable safety profile and was well-tolerated in participants carrying GRN or C9orf72 mutation causative of FTD.

Adverse event reporting additional description:

In total, 31 out of 33 (93.9%) participants experienced a TEAE of which 75.8% had mild or moderate TEAEs in severity; no treatment-related TEAEs were considered severe (or worse) in severity. There were no treatment-related TESAEs observed in the study and of the 6 TESAEs, one was fatal.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.1.
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Reporting groups

Reporting group title	aFTD-GRN
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Reporting group description: -

Reporting group title	FTD-GRN
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Reporting group description: -

Reporting group title	FTD-C9orf72
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Reporting group description: -

Serious adverse events	aFTD-GRN	FTD-GRN	FTD-C9orf72
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	3 / 12 (25.00%)	2 / 16 (12.50%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lip and/or oral cavity cancer			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (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
Injury, poisoning and procedural complications			
Procedural pneumothorax			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (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
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (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			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (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
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	aFTD-GRN	FTD-GRN	FTD-C9orf72
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	9 / 12 (75.00%)	13 / 16 (81.25%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic keratosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Diastolic hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypertension			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Subclavian artery occlusion subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
General disorders and administration site conditions			
Administration site extravasation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Crying subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Fatigue subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Infusion site extravasation subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Infusion site pain subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Infusion site paraesthesia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Immune system disorders			
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Asthma subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Epistaxis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Actinic keratosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Depression			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hallucination, auditory			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Illusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Impulsive behaviour			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Paranoia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Restlessness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Sleep disorder subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Product issues Device physical property issue subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Investigations Blood cholesterol increased subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Blood potassium increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Lipase increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Weight decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Injury, poisoning and procedural complications Alcohol poisoning subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Arthropod bite subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1

Fall			
subjects affected / exposed	2 / 5 (40.00%)	5 / 12 (41.67%)	7 / 16 (43.75%)
occurrences (all)	2	5	7
Head injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Patella fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Procedural pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Procedural pneumothorax			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sunburn			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Weight increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1	1 / 16 (6.25%) 1
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Aortic valve stenosis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Mitral valve incompetence subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 12 (8.33%) 1	0 / 16 (0.00%) 0
Nervous system disorders			
Aphasia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Carotid artery stenosis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 2	0 / 12 (0.00%) 0	0 / 16 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	1 / 12 (8.33%) 1	2 / 16 (12.50%) 2
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Lacunar infarction subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Lacunar stroke subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Myoclonus			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Parkinsonian rest tremor			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Polyneuropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Seizure like phenomena			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Subdural hygroma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Blepharitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Episcleritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Retinal detachment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dysphagia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Pancreatitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	2 / 16 (12.50%)
occurrences (all)	0	1	2
Ecchymosis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Intertrigo			

subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Photodermatosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pseudofolliculitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Psoriasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nocturia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 5 (0.00%)	2 / 12 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Urge incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Goitre			

subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 5 (40.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Bursitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Costochondritis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Medial tibial stress syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Osteoarthritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tendon disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Trigger finger			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 12 (0.00%) 0	1 / 16 (6.25%) 1
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Asymptomatic COVID-19			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	2 / 5 (40.00%)	0 / 12 (0.00%)	5 / 16 (31.25%)
occurrences (all)	2	0	5
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Eye infection bacterial			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Herpes simplex			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lyme disease			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Onychomycosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Otitis externa			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 5 (40.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Urinary tract infection			
subjects affected / exposed	1 / 5 (20.00%)	2 / 12 (16.67%)	6 / 16 (37.50%)
occurrences (all)	1	2	6
Viral rhinitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 12 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Eye contusion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 12 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0

Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gout			
subjects affected / exposed	0 / 5 (0.00%)	1 / 12 (8.33%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 April 2019	Protocol Version 1.0 - Original Protocol
22 April 2019	Protocol Version 1.1 Removed UPDRS Part III Clinical Outcome Assessment (COA), replaced "PPD" with "the CRO", and corrected inclusion/exclusion criteria numbering
24 June 2019	Protocol Version 1.2 Additional criteria added for withdrawal from study drug; language around infusion and injection-related reactions updated to align with Investigator's Brochure; clarification on AE and SAE reporting
02 August 2019	Protocol Version 1.3 Inclusion of independent Data Monitoring Committee (DMC)
12 September 2019	Protocol Version 1.4 Expanded risk/benefit assessment; clarification to the language regarding withdrawal from study and withdrawal from study drug
26 September 2019	Protocol Version 2.0 Updated terminology of Clinical Outcomes Assessments (COAs); addition of optional Open Label Extension (OLE), clarification of inclusion/exclusion criteria, updates to Schedule of Assessments
13 December 2019	Protocol Version 1.5 Administrative updates to the study team and clarification on reporting timeline for SAEs
02 June 2020	Protocol Version 3.0 Duration of treatment period expanded from 46 to 96 weeks; update to number of planned participants; updates to Schedule of Assessments and Statistical Analyses; addition of appendix to describe risk review and adaptations as a result of COVID-19
13 July 2020	Protocol Version 3.1 Update to AE definitions and pregnancy reporting instructions; update to COVID-19 pandemic language; minor formatting changes
23 November 2020	Protocol Version 3.2 Background information updated based on current IB; addition of protocol-specific instructions for reporting AEs related to disease progression
04 February 2021	Protocol Version 4.0 Added a Part 2 optional OLE period including updated study objectives, endpoints and assessments; updated relevant section with data from completed trial; safety follow-up period changed from 8-weeks to 10-weeks

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported.

Notes: