Clinical trial results:
A Randomized, Parallel-Arm, Double-Blind, Placebo-Controlled Study with Open-Label Extension to Assess the Efficacy and Safety of Vatiquinone for the Treatment of Friedreich Ataxia (MOVE-FA)

Summary

EudraCT number	2020-002812-36
Trial protocol	DE ES FR IT
Global end of trial date	02 October 2023

Results information

Result version number	v1 (current)
This version publication date	17 April 2024
First version publication date	17 April 2024

Trial information

Trial identification

Sponsor protocol code	PTC743-NEU-003-FA

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04577352
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PTC Therapeutics, Inc.
Sponsor organisation address	PTC Therapeutics, Inc., 100 Corporate Court, South Plainfield, United States, NJ 07080
Public contact	Medical Information, PTC Therapeutics International Limited, +353 19068700, medinfo@ptcbio.com
Scientific contact	PTC Therapeutics, Inc., Medical Information, +011 44 1-866-562-4620, medinfo@ptcbio.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001238-PIP03-21
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy (using the modified Friedreich Ataxia Rating Scale [mFARS]) and safety of vatiquinone in participants with Friedreich Ataxia (FA).

Protection of trial subjects:

This trial was designed and monitored in accordance with sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 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	Australia: 5
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Italy: 10
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Brazil: 16
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	United States: 64
Worldwide total number of subjects	146
EEA total number of subjects	35

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)	31
Adolescents (12-17 years)	69
Adults (18-64 years)	44
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study included a double-blind, placebo-controlled phase and an open-label extension phase.

Period 1

Period 1 title	Double-blind Phase (72 Weeks)
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	Vatiquinone

Arm description:

Participants received vatiquinone capsule at a dose of either 200 milligrams (mg) orally 3 times a day (TID) if 12 years of age and weighing 25 kilograms (kg) or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 72 weeks during the double-blind phase and for 24 weeks during the open-label phase.

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

Dosage and administration details:

Vatiquinone was administered per dose and schedule specified in the arm description.

Arm title	Placebo

Arm description:

Participants received placebo matching to vatiquinone (per age and weight) orally TID for 72 weeks during the double-blind phase and vatiquinone at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 24 weeks during the open-label phase.

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

Dosage and administration details:

Placebo matched to vatiquinone was administered per schedule specified in the arm description.

Number of subjects in period 1	Vatiquinone	Placebo
Started	73	73
Received at least 1 dose of study drug	73	73
Completed	63	65
Not completed	10	8
Consent withdrawn by subject	3	2
Adverse event, non-fatal	6	3
Death	-	1
Other than specified	1	1
Protocol deviation	-	1

Period 2

Period 2 title	Open-label Phase (24 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Vatiquinone

Arm description:

Participants received vatiquinone capsule at a dose of either 200 milligrams (mg) orally 3 times a day (TID) if 12 years of age and weighing 25 kilograms (kg) or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 72 weeks during the double-blind phase and for 24 weeks during the open-label phase.

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

Dosage and administration details:

Vatiquinone was administered per dose and schedule specified in the arm description.

Arm title	Placebo

Arm description:

Participants received placebo matching to vatiquinone (per age and weight) orally TID for 72 weeks during the double-blind phase and vatiquinone at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 24 weeks during the open-label phase.

Arm type	Placebo
Investigational medicinal product name	Vatiquinone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, Capsule
Routes of administration	Oral use, Oral use

Dosage and administration details:
Vatiquinone was administered per dose and schedule specified in the arm description.

Number of subjects in period 2	Vatiquinone	Placebo
Started	63	65
Received at least 1 dose of study drug	63	65
Completed	63	62
Not completed	0	3
Adverse event, non-fatal	-	2
Other than specified	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Vatiquinone
Reporting group description:	
Participants received vatiquinone capsule at a dose of either 200 milligrams (mg) orally 3 times a day (TID) if 12 years of age and weighing 25 kilograms (kg) or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 72 weeks during the double-blind phase and for 24 weeks during the open-label phase.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching to vatiquinone (per age and weight) orally TID for 72 weeks during the double-blind phase and vatiquinone at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 24 weeks during the open-label phase.	

Reporting group values	Vatiquinone	Placebo	Total
Number of subjects	73	73	146
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	18.9	18.2	
standard deviation	± 12.24	± 11.27	-
Gender Categorical Units: Subjects			
Female	45	42	87
Male	28	31	59
Ethnicity Units: Subjects			
Hispanic or Latino	10	9	19
Not Hispanic or Latino	63	63	126
Not Reported	0	1	1
Race Units: Subjects			
White	68	69	137
Other	5	4	9

End points

End points reporting groups

Reporting group title	Vatiquinone
Reporting group description:	
Participants received vatiquinone capsule at a dose of either 200 milligrams (mg) orally 3 times a day (TID) if 12 years of age and weighing 25 kilograms (kg) or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 72 weeks during the double-blind phase and for 24 weeks during the open-label phase.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching to vatiquinone (per age and weight) orally TID for 72 weeks during the double-blind phase and vatiquinone at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 24 weeks during the open-label phase.	
Reporting group title	Vatiquinone
Reporting group description:	
Participants received vatiquinone capsule at a dose of either 200 milligrams (mg) orally 3 times a day (TID) if 12 years of age and weighing 25 kilograms (kg) or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 72 weeks during the double-blind phase and for 24 weeks during the open-label phase.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matching to vatiquinone (per age and weight) orally TID for 72 weeks during the double-blind phase and vatiquinone at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 24 weeks during the open-label phase.	

Primary: Change From Baseline in the mFARS Score at Week 72 - Modified Intent-to-treat (mITT) Analysis Set

End point title	Change From Baseline in the mFARS Score at Week 72 - Modified Intent-to-treat (mITT) Analysis Set
End point description:	
mFARS is a 93-item scale; comprised of neurologic component of Friedreich Ataxia Rating Scale (FARS). For each item, responses categorize the corresponding neurological finding, with a score ranging from 0 to 3, 4, or 5 with 0 being normal and higher numbers indicative of greater impairment. Total mFARS scores for each subscale: bulbar (0 to 5), upper limb coordination (0 to 36), lower limb coordination (0 to 16), and upright stability (0 to 36). mFARS total score was a composite score of all 4 subscales, ranging from 0 (normal) to 93 (greater impairment). A lower score = better neurological function. Missing data was imputed using pattern mix model multiple imputation. Least square (LS) mean and standard error (SE) was calculated using mixed-model repeated measures (MMRM). The mITT analysis set included all randomized participants, between age of 7 and 21 years who received at least 1 dose of study drug, had baseline and at least 1 postbaseline measurement of primary endpoint.	
End point type	Primary
End point timeframe:	
Baseline, Week 72	

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: units on a scale				
least squares mean (standard error)	1.218 (± 0.9652)	2.828 (± 0.9994)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.144
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.769
upper limit	0.55
Variability estimate	Standard error of the mean
Dispersion value	1.1016

Primary: Change From Baseline in the mFARS Score at Week 72 - Intent-to-treat (ITT) Analysis Set

End point title	Change From Baseline in the mFARS Score at Week 72 - Intent-to-treat (ITT) Analysis Set

End point description:

mFARS is a 93-item scale; comprised of neurologic component of FARS. For each item, responses categorize the corresponding neurological finding, with a score ranging from 0 to 3, 4, or 5 with 0 being normal and higher numbers indicative of greater impairment. Total mFARS scores for each subscale: bulbar (0 to 5), upper limb coordination (0 to 36), lower limb coordination (0 to 16), and upright stability (0 to 36). mFARS total score was a composite score of all 4 subscales, ranging from 0 (normal) to 93 (greater impairment). A lower score = better neurological function. Missing data was imputed using pattern mix model multiple imputation. LS mean and SE was calculated using MMRM. The ITT analysis set included all randomized participants who had received at least 1 dose of study drug (vatiquinone or placebo), and had baseline and at least 1 postbaseline measurement of the primary endpoint.

End point type	Primary

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	73		
Units: units on a scale				
least squares mean (standard error)	0.898 (± 0.8500)	2.555 (± 0.8770)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0984
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.657
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.622
upper limit	0.308
Variability estimate	Standard error of the mean
Dispersion value	1.0027

Secondary: Change From Baseline in FARS-ADL Score at Week 72 - ITT Analysis Set

End point title	Change From Baseline in FARS-ADL Score at Week 72 - ITT Analysis Set

End point description:

The ADL component of the FARS includes 9 subscales: speech, swallowing, cutting food and handling utensils, dressing, personal hygiene, falling, walking, quality of sitting position, and bladder function. Each of these subscales is rated on a 5-point scale where 0=normal to 4=severe disability/inability to carry out activity independently for a total possible score of 0 to 36, with higher scores representing greater disability/dependency. Missing data was imputed using pattern mix model multiple imputation. LS mean and SE was calculated using MMRM. The ITT analysis set included all randomized participants who had received at least 1 dose of study drug (vatiquinone or placebo), and had baseline and at least 1 postbaseline measurement of the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	73		
Units: units on a scale				
least squares mean (standard error)	0.707 (± 0.5219)	1.692 (± 0.5402)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.082
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.985
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.095
upper limit	0.125
Variability estimate	Standard error of the mean
Dispersion value	0.5664

Secondary: Change From Baseline in Friedreich Ataxia Rating Scale Activities of Daily Living (FARS-ADL) Score at Week 72 - mITT Analysis Set

End point title	Change From Baseline in Friedreich Ataxia Rating Scale Activities of Daily Living (FARS-ADL) Score at Week 72 - mITT Analysis Set

End point description:

The ADL component of the FARS includes 9 subscales: speech, swallowing, cutting food and handling utensils, dressing, personal hygiene, falling, walking, quality of sitting position, and bladder function. Each of these subscales is rated on a 5-point scale where 0=normal to 4=severe disability/inability to carry out activity independently for a total possible score of 0 to 36, with higher scores representing greater disability/dependency. Missing data was imputed using pattern mix model multiple imputation. LS mean and SE was calculated using MMRM. The mITT analysis set included all randomized participants, between age of 7 and 21 years, inclusive, at Screening, had received at least 1 dose of study drug, had baseline and at least 1 post-baseline measurement of the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: units on a scale				
least squares mean (standard error)	0.759 (± 0.5992)	1.677 (± 0.6202)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1382
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.918
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.132
upper limit	0.296
Variability estimate	Standard error of the mean
Dispersion value	0.6194

Secondary: Change From Baseline in 1-Minute Walk Test (1MWT) at Week 72 - mITT Analysis Set

End point title	Change From Baseline in 1-Minute Walk Test (1MWT) at Week 72 - mITT Analysis Set

End point description:

The 1MWT is a timed performance test used to measure functional ability, walking endurance, balance, and muscle performance by measuring maximal walking speed in 1 minute. Participants were instructed to walk as quickly as possible for 1 minute without running. Maximal walking speed was measured upon completion of the walk and distance was recorded. Missing data was imputed using pattern mix model multiple imputation. LS mean and SE was calculated using MMRM. The mITT analysis set included all randomized participants, between age of 7 and 21 years, inclusive, at Screening, had received at least 1 dose of study drug, had baseline and at least 1 post-baseline measurement of the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: meters				
least squares mean (standard error)	-4.324 (± 2.5882)	-9.290 (± 2.6843)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.08
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	4.966
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.593
upper limit	10.525
Variability estimate	Standard error of the mean
Dispersion value	2.8363

Secondary: Change From Baseline in 1MWT at Week 72 - ITT Analysis Set

End point title	Change From Baseline in 1MWT at Week 72 - ITT Analysis Set

End point description:

The 1MWT is a timed performance test used to measure functional ability, walking endurance, balance, and muscle performance by measuring maximal walking speed in 1 minute. Participants were instructed to walk as quickly as possible for 1 minute without running. Maximal walking speed was measured upon completion of the walk and distance was recorded. Missing data was imputed using pattern mix model multiple imputation. LS mean and SE was calculated using MMRM. The ITT analysis set included all randomized participants who had received at least 1 dose of study drug (vatiquinone or placebo), and had baseline and at least 1 postbaseline measurement of the primary endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	73		
Units: meters				
least squares mean (standard error)	-4.623 (± 2.2113)	-9.462 (± 2.2687)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0551
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	4.839
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.106
upper limit	9.784
Variability estimate	Standard error of the mean
Dispersion value	2.5231

Secondary: Number of Falls per 28 Days over Every 24-Week Period - mITT Analysis Set

End point title	Number of Falls per 28 Days over Every 24-Week Period - mITT Analysis Set

End point description:

Each participant was required to maintain a fall log, which included the date and time of each fall. Falls as defined by World Health Organization as "inadvertently coming to rest on the ground, floor or other lower level, excluding intentional change in position to rest in furniture, wall or other objects," were reported. Number of falls per 28 days during a time interval was calculated as the number of falls during the period divided by the number of days during the interval, and multiplied by 28. The falls that occurred on or after the first Loss of Ambulation visit were excluded from the analysis. The mITT analysis set included all randomized participants, between age of 7 and 21 years, inclusive, at Screening, had received at least 1 dose of study drug, had baseline and at least 1 post-baseline measurement of the primary endpoint. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Week 1-24, Week 25-48, and Week 49-72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	62		
Units: falls				
arithmetic mean (standard deviation)				
Week 1-24 (n = 60, 62)	5.029 (± 14.4686)	3.999 (± 6.9569)		
Week 25-48 (n = 56, 60)	4.098 (± 11.5289)	3.900 (± 9.0212)		
Week 49-72 (n = 54, 57)	3.732 (± 10.0790)	4.462 (± 12.1785)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Falls per 28 Days over Every 24-Week Period - ITT Analysis Set

End point title	Number of Falls per 28 Days over Every 24-Week Period - ITT Analysis Set

End point description:

Each participant was required to maintain a fall log, which included the date and time of each fall. Falls as defined by World Health Organization as "inadvertently coming to rest on the ground, floor or other lower level, excluding intentional change in position to rest in furniture, wall or other objects," were reported. Number of falls per 28 days during a time interval was calculated as the number of falls during the period divided by the number of days during the interval, and multiplied by 28. The falls that occurred on or after the first Loss of Ambulation visit were excluded from the analysis. The ITT analysis set included all randomized participants who had received at least 1 dose of study drug (vatiquinone or placebo), and had baseline and at least 1 postbaseline measurement of the primary endpoint. 'Overall number of participants analyzed' = participants evaluable for this endpoint. 'n' = participants evaluable at specified timepoint.

End point type	Secondary

End point timeframe:

Week 1-24, Week 25-48, and Week 49-72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	73		
Units: falls				
arithmetic mean (standard deviation)				
Week 1-24 (n = 69, 73)	4.464 (± 13.5618)	3.535 (± 6.5231)		
Week 25-48 (n = 63, 69)	3.920 (± 10.9850)	3.518 (± 8.4701)		
Week 49-72 (n = 60, 65)	3.407 (± 9.6043)	3.974 (± 11.4690)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in the Upright Stability Subscale of the mFARS at Week 72 - mITT Analysis Set

End point title	Change From Baseline in the Upright Stability Subscale of the mFARS at Week 72 - mITT Analysis Set

End point description:

mFARS is a 93-item scale; comprised of neurologic component of FARS. For each item, responses categorize the corresponding neurological finding, with a score ranging from 0 to 3, 4, or 5 with 0 being normal and higher numbers indicative of greater impairment. The upright stability subscale score ranges from 0 (normal) to 36 (greater impairment). A lower score = better neurological function. Missing data was imputed using pattern mix model multiple imputation. LS mean and SE was calculated using MMRM. The mITT analysis set included all randomized participants, between age of 7 and 21 years who received at least 1 dose of study drug, had baseline and at least 1 postbaseline measurement of primary endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: units on a scale				
least squares mean (standard error)	1.734 (± 0.4911)	2.991 (± 0.5094)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0212
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.257
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.325
upper limit	-0.188
Variability estimate	Standard error of the mean
Dispersion value	0.5453

Other pre-specified: Change From Baseline in the Upright Stability Subscale of the

mFARS at Week 72 - ITT Analysis Set

End point title	Change From Baseline in the Upright Stability Subscale of the mFARS at Week 72 - ITT Analysis Set

End point description:

mFARS is a 93-item scale; comprised of neurologic component of FARS. For each item, responses categorize the corresponding neurological finding, with a score ranging from 0 to 3, 4, or 5 with 0 being normal and higher numbers indicative of greater impairment. The upright stability subscale score ranges from 0 (normal) to 36 (greater impairment). A lower score = better neurological function. Missing data was imputed using pattern mix model multiple imputation. LS mean and SE was calculated using MMRM. The ITT analysis set included all randomized participants who had received at least 1 dose of study drug (vatiquinone or placebo), and had baseline and at least 1 postbaseline measurement of the primary endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	73		
Units: units on a scale				
least squares mean (standard error)	1.379 (± 0.4321)	2.489 (± 0.4468)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0246
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.079
upper limit	-0.142
Variability estimate	Standard error of the mean
Dispersion value	0.4941

Other pre-specified: Change From Baseline in the Modified Fatigue Impact Scale (MFIS) Score at Week 72 - mITT Analysis Set

End point title	Change From Baseline in the Modified Fatigue Impact Scale (MFIS) Score at Week 72 - mITT Analysis Set

End point description:

The MFIS is a 21-item, reliable, validated instrument that has been utilized in many neurological disorders. It is a modified form of the Fatigue Impact Scale, a component of the Multiple Sclerosis Quality of Life Inventory. Each item was scored on a scale of 0 (never) to 4 (almost always). The total score was the sum of all item's score and ranged from 0 (no fatigue impact) to 84 (almost always impacted by fatigue). Higher scores indicated greater impact of fatigue on participant function. The mITT analysis set included all randomized participants, between age of 7 and 21 years who received at least 1 dose of study drug, had baseline and at least 1 postbaseline measurement of primary endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, Week 72

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	62		
Units: units on a scale				
least squares mean (standard error)	-0.756 (± 2.2197)	4.291 (± 2.3344)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0252
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-5.048
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.468
upper limit	-0.628
Variability estimate	Standard error of the mean
Dispersion value	2.255

Other pre-specified: Change From Baseline in the MFIS Score at Week 72 - ITT Analysis Set

End point title	Change From Baseline in the MFIS Score at Week 72 - ITT Analysis Set

End point description:

The MFIS is a 21-item, reliable, validated instrument that has been utilized in many neurological disorders. It is a modified form of the Fatigue Impact Scale, a component of the Multiple Sclerosis Quality of Life Inventory. Each item was scored on a scale of 0 (never) to 4 (almost always). The total score was the sum of all item's score and ranged from 0 (no fatigue impact) to 84 (almost always

impacted by fatigue). Higher scores indicated greater impact of fatigue on participant function. The ITT analysis set included all randomized participants who had received at least 1 dose of study drug (vatiquinone or placebo), and had baseline and at least 1 postbaseline measurement of the primary endpoint.

End point type	Other pre-specified
End point timeframe:	
Baseline, Week 72	

End point values	Vatiquinone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	73		
Units: units on a scale				
least squares mean (standard error)	-1.200 (± 1.9897)	4.354 (± 2.0758)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vatiquinone v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0095
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-5.554
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.75
upper limit	-1.358
Variability estimate	Standard error of the mean
Dispersion value	2.1409

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 100

Adverse event reporting additional description:

Double-blind phase: The safety analysis set included all participants who received at least 1 dose of study drug.
On-Vatiquinone period: On-Vatiquinone safety analysis set included all randomized participants who received at least 1 dose of Vatiquinone anytime during the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Double-blind Phase: Vatiquinone

Reporting group description:

Participants received vatiquinone capsule at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 72 weeks during the double-blind phase.

Reporting group title	On-Vatiquinone Period: Placebo/Vatiquinone

Reporting group description:

Participants who received placebo for 72 weeks in the double-blind phase, received vatiquinone at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 24 weeks during the open-label phase.

Reporting group title	On-Vatiquinone Period: Vatiquinone/Vatiquinone

Reporting group description:

Participants who received vatiquinone for 72 weeks in the double-blind phase continued to receive vatiquinone capsule at a dose of either 200 mg orally TID if 12 years of age and weighing 25 kg or 400 mg orally TID if ≥12 years of age and/or weighing ≥25 kg for 24 weeks during the open-label phase.

Reporting group title	Double-blind Phase: Placebo

Reporting group description:

Participants received placebo matching to vatiquinone (per age and weight) orally TID for 72 weeks during the double-blind phase.

Serious adverse events	Double-blind Phase: Vatiquinone	On-Vatiquinone Period: Placebo/Vatiquinone	On-Vatiquinone Period: Vatiquinone/Vatiquinone
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 73 (10.96%)	2 / 65 (3.08%)	10 / 73 (13.70%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Intentional product misuse			

subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 73 (0.00%)	1 / 65 (1.54%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Multisystem inflammatory syndrome in children			

subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 73 (0.00%)	1 / 65 (1.54%)	0 / 73 (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
Nausea			
subjects affected / exposed	0 / 73 (0.00%)	1 / 65 (1.54%)	0 / 73 (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
Impaired gastric emptying			
subjects affected / exposed	0 / 73 (0.00%)	1 / 65 (1.54%)	0 / 73 (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			
Suicide attempt			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			

subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 73 (0.00%)	1 / 65 (1.54%)	0 / 73 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Type 2 diabetes mellitus			
subjects affected / exposed	0 / 73 (0.00%)	0 / 65 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Double-blind Phase: Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 73 (10.96%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Intentional product misuse			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Myocarditis			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			

subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Multisystem inflammatory syndrome in children			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Impaired gastric emptying			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide attempt			

subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Anxiety			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis perforated			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Urinary tract infection			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Double-blind Phase: Vatiquinone	On-Vatiquinone Period: Placebo/Vatiquinone	On-Vatiquinone Period: Vatiquinone/Vatiquinone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 73 (97.26%)	53 / 65 (81.54%)	71 / 73 (97.26%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 73 (5.48%)	2 / 65 (3.08%)	5 / 73 (6.85%)
occurrences (all)	4	2	5
Fatigue			
subjects affected / exposed	9 / 73 (12.33%)	3 / 65 (4.62%)	11 / 73 (15.07%)
occurrences (all)	12	3	14
Reproductive system and breast disorders			
Dysmenorrhoea			

subjects affected / exposed	4 / 73 (5.48%)	0 / 65 (0.00%)	4 / 73 (5.48%)
occurrences (all)	9	0	9
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	6 / 73 (8.22%)	0 / 65 (0.00%)	8 / 73 (10.96%)
occurrences (all)	8	0	10
Oropharyngeal pain			
subjects affected / exposed	8 / 73 (10.96%)	3 / 65 (4.62%)	8 / 73 (10.96%)
occurrences (all)	11	4	11
Cough			
subjects affected / exposed	5 / 73 (6.85%)	1 / 65 (1.54%)	5 / 73 (6.85%)
occurrences (all)	5	1	5
Rhinorrhoea			
subjects affected / exposed	4 / 73 (5.48%)	1 / 65 (1.54%)	4 / 73 (5.48%)
occurrences (all)	4	1	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 73 (6.85%)	1 / 65 (1.54%)	6 / 73 (8.22%)
occurrences (all)	5	1	6
Investigations			
Weight increased			
subjects affected / exposed	0 / 73 (0.00%)	1 / 65 (1.54%)	1 / 73 (1.37%)
occurrences (all)	0	1	1
International normalised ratio increased			
subjects affected / exposed	3 / 73 (4.11%)	0 / 65 (0.00%)	4 / 73 (5.48%)
occurrences (all)	3	0	4
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 73 (2.74%)	1 / 65 (1.54%)	2 / 73 (2.74%)
occurrences (all)	2	1	2
Fall			
subjects affected / exposed	58 / 73 (79.45%)	34 / 65 (52.31%)	59 / 73 (80.82%)
occurrences (all)	363	89	468
Ligament sprain			

subjects affected / exposed	4 / 73 (5.48%)	0 / 65 (0.00%)	4 / 73 (5.48%)
occurrences (all)	4	0	4
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 73 (1.37%)	0 / 65 (0.00%)	1 / 73 (1.37%)
occurrences (all)	1	0	1
Nervous system disorders			
Balance disorder			
subjects affected / exposed	2 / 73 (2.74%)	0 / 65 (0.00%)	2 / 73 (2.74%)
occurrences (all)	2	0	2
Dizziness			
subjects affected / exposed	11 / 73 (15.07%)	7 / 65 (10.77%)	12 / 73 (16.44%)
occurrences (all)	15	8	18
Headache			
subjects affected / exposed	22 / 73 (30.14%)	7 / 65 (10.77%)	25 / 73 (34.25%)
occurrences (all)	37	9	43
Syncope			
subjects affected / exposed	4 / 73 (5.48%)	1 / 65 (1.54%)	4 / 73 (5.48%)
occurrences (all)	4	1	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	19 / 73 (26.03%)	5 / 65 (7.69%)	21 / 73 (28.77%)
occurrences (all)	28	5	31
Dyspepsia			
subjects affected / exposed	4 / 73 (5.48%)	1 / 65 (1.54%)	5 / 73 (6.85%)
occurrences (all)	8	1	10
Nausea			
subjects affected / exposed	13 / 73 (17.81%)	5 / 65 (7.69%)	15 / 73 (20.55%)
occurrences (all)	16	8	19
Abdominal pain			
subjects affected / exposed	10 / 73 (13.70%)	1 / 65 (1.54%)	10 / 73 (13.70%)
occurrences (all)	15	1	15
Abdominal pain upper			
subjects affected / exposed	7 / 73 (9.59%)	8 / 65 (12.31%)	8 / 73 (10.96%)
occurrences (all)	9	14	11
Odynophagia			

subjects affected / exposed	2 / 73 (2.74%)	0 / 65 (0.00%)	2 / 73 (2.74%)
occurrences (all)	2	0	2
Vomiting			
subjects affected / exposed	14 / 73 (19.18%)	7 / 65 (10.77%)	17 / 73 (23.29%)
occurrences (all)	17	10	21
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	3 / 73 (4.11%)	2 / 65 (3.08%)	4 / 73 (5.48%)
occurrences (all)	4	2	6
Pruritus			
subjects affected / exposed	3 / 73 (4.11%)	0 / 65 (0.00%)	5 / 73 (6.85%)
occurrences (all)	3	0	5
Rash			
subjects affected / exposed	4 / 73 (5.48%)	0 / 65 (0.00%)	5 / 73 (6.85%)
occurrences (all)	4	0	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 73 (8.22%)	1 / 65 (1.54%)	7 / 73 (9.59%)
occurrences (all)	7	1	9
Back pain			
subjects affected / exposed	7 / 73 (9.59%)	1 / 65 (1.54%)	9 / 73 (12.33%)
occurrences (all)	8	1	14
Muscle spasms			
subjects affected / exposed	3 / 73 (4.11%)	2 / 65 (3.08%)	4 / 73 (5.48%)
occurrences (all)	3	2	4
Myalgia			
subjects affected / exposed	3 / 73 (4.11%)	0 / 65 (0.00%)	3 / 73 (4.11%)
occurrences (all)	3	0	3
Pain in extremity			
subjects affected / exposed	9 / 73 (12.33%)	1 / 65 (1.54%)	9 / 73 (12.33%)
occurrences (all)	11	1	11
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	5 / 73 (6.85%)	1 / 65 (1.54%)	5 / 73 (6.85%)
occurrences (all)	5	1	5
Influenza			

subjects affected / exposed	8 / 73 (10.96%)	2 / 65 (3.08%)	9 / 73 (12.33%)
occurrences (all)	9	2	10
Nasopharyngitis			
subjects affected / exposed	12 / 73 (16.44%)	6 / 65 (9.23%)	12 / 73 (16.44%)
occurrences (all)	19	9	20
Gastroenteritis			
subjects affected / exposed	3 / 73 (4.11%)	1 / 65 (1.54%)	4 / 73 (5.48%)
occurrences (all)	3	1	4
COVID-19			
subjects affected / exposed	32 / 73 (43.84%)	4 / 65 (6.15%)	36 / 73 (49.32%)
occurrences (all)	36	5	41
Sinusitis			
subjects affected / exposed	4 / 73 (5.48%)	0 / 65 (0.00%)	4 / 73 (5.48%)
occurrences (all)	5	0	5
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 73 (5.48%)	0 / 65 (0.00%)	4 / 73 (5.48%)
occurrences (all)	4	0	4
Viral rhinitis			
subjects affected / exposed	8 / 73 (10.96%)	1 / 65 (1.54%)	11 / 73 (15.07%)
occurrences (all)	18	1	24
Viral infection			
subjects affected / exposed	3 / 73 (4.11%)	2 / 65 (3.08%)	4 / 73 (5.48%)
occurrences (all)	3	2	4
Urinary tract infection			
subjects affected / exposed	3 / 73 (4.11%)	1 / 65 (1.54%)	6 / 73 (8.22%)
occurrences (all)	3	1	6
Upper respiratory tract infection			
subjects affected / exposed	9 / 73 (12.33%)	8 / 65 (12.31%)	12 / 73 (16.44%)
occurrences (all)	17	9	24
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 73 (6.85%)	1 / 65 (1.54%)	5 / 73 (6.85%)
occurrences (all)	6	1	6

Non-serious adverse events	Double-blind Phase: Placebo		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	73 / 73 (100.00%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	9 / 73 (12.33%)		
occurrences (all)	14		
Fatigue			
subjects affected / exposed	13 / 73 (17.81%)		
occurrences (all)	21		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	4		
Oropharyngeal pain			
subjects affected / exposed	8 / 73 (10.96%)		
occurrences (all)	11		
Cough			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	6		
Rhinorrhoea			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	5		
Investigations			
Weight increased			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	6		
International normalised ratio increased			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	6		
Fall			
subjects affected / exposed	61 / 73 (83.56%)		
occurrences (all)	441		
Ligament sprain			
subjects affected / exposed	5 / 73 (6.85%)		
occurrences (all)	5		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	6		
Nervous system disorders			
Balance disorder			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	4		
Dizziness			
subjects affected / exposed	8 / 73 (10.96%)		
occurrences (all)	8		
Headache			
subjects affected / exposed	26 / 73 (35.62%)		
occurrences (all)	53		
Syncope			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 73 (13.70%)		
occurrences (all)	12		
Dyspepsia			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	3		
Nausea			

subjects affected / exposed	10 / 73 (13.70%)		
occurrences (all)	16		
Abdominal pain			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	7		
Abdominal pain upper			
subjects affected / exposed	10 / 73 (13.70%)		
occurrences (all)	17		
Odynophagia			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	9 / 73 (12.33%)		
occurrences (all)	13		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	3		
Pruritus			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	5 / 73 (6.85%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	8		
Muscle spasms			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	7		
Myalgia			

subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	7 / 73 (9.59%)		
occurrences (all)	10		
Infections and infestations			
Gastroenteritis viral			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	5		
Influenza			
subjects affected / exposed	11 / 73 (15.07%)		
occurrences (all)	13		
Nasopharyngitis			
subjects affected / exposed	17 / 73 (23.29%)		
occurrences (all)	34		
Gastroenteritis			
subjects affected / exposed	4 / 73 (5.48%)		
occurrences (all)	4		
COVID-19			
subjects affected / exposed	24 / 73 (32.88%)		
occurrences (all)	26		
Sinusitis			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	2		
Viral rhinitis			
subjects affected / exposed	3 / 73 (4.11%)		
occurrences (all)	4		
Viral infection			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	2 / 73 (2.74%)		
occurrences (all)	4		

Upper respiratory tract infection subjects affected / exposed occurrences (all)	8 / 73 (10.96%) 10		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	3 / 73 (4.11%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 August 2020	The overall reasons of this amendment was to revise the length of the placebo-controlled portion of the trial from 48 weeks to 72 weeks and the open-label portion from 48 weeks to 24 weeks.
03 March 2021	The overall reasons of this amendment was to clarify unblinding procedures, clarify disease worsening as a reason for discontinuation from study treatment, add a table of prohibited medications and add text clarifying the volume of blood that will be drawn during the study.
15 April 2021	The overall reasons of this amendment was to add risk/benefit language with regard to the pediatric population, revise the timing of the follow up visit from 10 to 30 days to approximately 30 days, and add details regarding maintaining the blind.
21 May 2021	The overall reason of this amendment was to clarify concomitant medication use and add exclusion of illicit drug use.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported