Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Global Phase 3 Study of Edasalonexent in Pediatric Patients With Duchenne Muscular Dystrophy

Summary

EudraCT number	2018-000464-29
Trial protocol	DE SE IE
Global end of trial date	22 September 2020

Results information

Result version number	v1 (current)
This version publication date	03 February 2022
First version publication date	03 February 2022

Trial information

Trial identification

Sponsor protocol code	CAT-1004-301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03703882
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astria Therapeutics, Inc
Sponsor organisation address	100 High Street, 28th Floor, Boston, MA, United States, 02110
Public contact	Andrew Nichols, PhD - Chief Scientific Officer, Astria Therapeutics, Inc, 001 617-349-1971, anichols@astriatx.com
Scientific contact	Andrew Nichols, PhD - Chief Scientific Officer, Astria Therapeutics, Inc, 001 617-349-1971, anichols@astriatx.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	13 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 September 2020
Global end of trial reached?	Yes
Global end of trial date	22 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of edasalonexent as measured by change from Baseline (CFB) on North Star Ambulatory Assessment (NSAA) Total Score in pediatric patients with Duchenne muscular dystrophy (DMD)

Protection of trial subjects:

This study was conducted in accordance with the protocol, Health Insurance Portability and Accountability Act (HIPAA) regulations, Food and Drug Administration (FDA) GCP Regulations (21 CFR Parts 50, 56, and 312) and ICH guidelines for GCP (E6) and clinical safety data management (E2A), and the ethical principles that had their origin in the Declaration of Helsinki. The study was conducted in accordance with applicable local law(s) and regulation(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 October 2018
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	Sweden: 4
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Ireland: 4
Country: Number of subjects enrolled	United States: 84
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Australia: 6
Worldwide total number of subjects	131
EEA total number of subjects	16

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)	131
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multi-center study conducted by 37 principal investigators at 37 study centers in 8 countries (United States, Canada, United Kingdom, Germany, Ireland, Israel, Sweden, and Australia).

Pre-assignment

Screening details:

A total of 151 patients were screened of which 20 failed screening. 131 patients who participated in the study included 126 randomized patients and 5 participants who were dosed siblings of previously randomized patients.

Period 1

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

Blinding implementation details:

Patients were randomized to receive edasalonexent 100 mg/kg/day (administered as approximately 33 mg/kg TID) or placebo in double-blind fashion daily for 52 weeks. Patients, investigators, study staff, and the Sponsor were blinded to study drug assignment. Prior to scheduled unblinding, if an emergency required the identity of the IP to be known by the Investigator in order to provide appropriate medical treatment, the Investigator was allowed to unblind using the Interactive Web Response System

Arms

Are arms mutually exclusive?	Yes
Arm title	Dose 1

Arm description:

Edasalonexent 100 mg/kg/day. Capsules taken by mouth three times per day.

Arm type	Experimental
Investigational medicinal product name	Edasalonexent
Investigational medicinal product code	
Other name	Edasa, CAT-1004
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received Edasalonexent 100 mg/kg/day. Capsules taken by mouth three times per day for 52 weeks.

Arm title	Placebo

Arm description:

Matching placebo

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:

Subjects received a placebo capsules taken by mouth three times per day for 52 weeks.

Number of subjects in period 1	Dose 1	Placebo
Started	88	43
Completed	85	37
Not completed	3	6
Consent withdrawn by subject	1	-
Physician decision	-	1
Adverse event, non-fatal	1	-
Starting another treatment	-	1
Progressive Disease	1	-
Non-compliance with study drug	-	1
Lost to follow-up	-	2
Non-compliance with study procedure	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Dose 1
Reporting group description:	
Edasalonexent 100 mg/kg/day. Capsules taken by mouth three times per day.	
Reporting group title	Placebo
Reporting group description:	
Matching placebo	

Reporting group values	Dose 1	Placebo	Total
Number of subjects	88	43	131
Age categorical			
Safety Population: All patients who received at least 1 dose of study drug, with patients analyzed based on the actual study treatment received. This included the set of patients who were assigned the same treatment as their randomized sibling.			
Units: Subjects			
Children (2-11 years)	88	43	131
Age continuous			
Safety Population: All patients who received at least 1 dose of study drug, with patients analyzed based on the actual study treatment received. This included the set of patients who were assigned the same treatment as their randomized sibling.			
Units: years			
arithmetic mean	5.65	5.77	
standard deviation	± 1.048	± 0.995	-
Gender categorical			
Safety Population: All patients who received at least 1 dose of study drug, with patients analyzed based on the actual study treatment received. This included the set of patients who were assigned the same treatment as their randomized sibling.			
Units: Subjects			
Female	0	0	0
Male	88	43	131
Ethnicity			
Safety Population: All patients who received at least 1 dose of study drug, with patients analyzed based on the actual study treatment received. This included the set of patients who were assigned the same treatment as their randomized sibling.			
Units: Subjects			
Hispanic or Latino	14	6	20
Not Hispanic or Latino	69	35	104
Unknown or Not Reported	5	2	7
Race			
Safety Population: All patients who received at least 1 dose of study drug, with patients analyzed based on the actual study treatment received. This included the set of patients who were assigned the same treatment as their randomized sibling. A patient who reported more than 1 race was categorized as multiracial.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	4	1	5
White	74	38	112

More than one race	3	1	4
Unknown or Not Reported	2	1	3
Missing-Race	1	0	1

End points

End points reporting groups

Reporting group title	Dose 1
Reporting group description:	
Edasalonexent 100 mg/kg/day. Capsules taken by mouth three times per day.	
Reporting group title	Placebo
Reporting group description:	
Matching placebo	

Primary: Change From Baseline in North Star Ambulatory Assessment (NSAA)

End point title	Change From Baseline in North Star Ambulatory Assessment (NSAA)

End point description:

To assess change from baseline in NSAA Total Score at Week 52. NSAA is a clinician-reported outcome instrument designed to measure ambulatory function in males with DMD. Patients asked to perform 17 different functional activities, including a 10MWT, rising from sit to stand, standing on one leg, climbing and descending a step, stand from supine, lifting the head, standing on heels, and jumping. Each function activity will be scored as 0=(unable to achieve independently), scored as 1=(modified method but achieves goal independent of physical assistance from another), or scored as 2 =(no obvious modification of activity) or "Not Scored". If the NSAA test was performed and any of the individual items are scored as "not scored" (i.e., for reasons unrelated to the patients physical capabilities), corresponding total score will be set to missing. sum of 17 scores will be used to form an ordinal total score (range 0 – 34).

Full Analysis population

End point type	Primary
End point timeframe:	
Baseline (Day 1) to Week 52	

End point values	Dose 1	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	38		
Units: score on a scale				
arithmetic mean (standard deviation)	-1.5 (± 4.41)	-1.8 (± 3.81)		

Statistical analyses

Statistical analysis title	Change From Baseline in NSAA
Statistical analysis description:	
Full Analysis population	
Comparison groups	Dose 1 v Placebo

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.6705 [2]
Method	ANCOVA

Notes:

[1] - The model includes change from baseline in the NSAA Total Score as the dependent variable, treatment, visit, and treatment-by-visit interaction as fixed effects, with baseline age, time to stand from supine, region (North America vs. Europe/Asia/Australia), and baseline NSAA score as covariates (including a by-visit interaction term for each covariate), and patient as a random effect.
[2] - Least Squares means, p-values from mixed-model repeated-measures(MMRM) ANCOVA.

Secondary: Change From Baseline in 10-meter Walk/Run Test

End point title	Change From Baseline in 10-meter Walk/Run Test

End point description:

To assess the changes from baseline to Week 52 on the 10-meter walk/run test (10MWT). For timed function tests (TFTs), the time will be set to 12 seconds and the speed to 0 if the TFT assessment meets the following TFT grading criteria. Grade of 1 or 2 (from a 6-point scale). 1=Unable to walk independently 2=Unable to walk independently but can walk with knee-ankle foot orthoses or support from a person 3=Highly adapted wide based lordotic gait. Cannot increase walking speed 4=Moderately adapted gait. Can pick up speed but cannot run 5=Able to pick up speed, but runs with a double stance phase, i.e. cannot achieve both feet off the ground 6=Runs and gets both feet off the ground (with no double stance phase)

Full Analysis population: All patients in the Randomized Population who received at least 1 dose of study drug and provided at least 1 valid post Baseline NSAA efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 52

End point values	Dose 1	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	38		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.0058 (± 0.03010)	-0.0093 (± 0.02538)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Stand From Supine

End point title	Change From Baseline in Time to Stand From Supine

End point description:

To assess the change from baseline in the stand from supine speed at Week 52. For timed function tests (TFTs) , the time will be set to 12 seconds and the speed to 0 if the TFT assessment meets the following TFT grading criteria. Grade of 1 or 2 (from a 6-point scale). 1 = Unable to stand from supine, even with use of a chair, 2 = Assisted Gowers -requires furniture for assist in arising from supine to full upright posture (no time to be recorded) 3=Rolls over, stands up with both hands "climbing up" the legs to achieve full upright posture 4=Rolls over, stands up with 1 hand support on leg 5=Rolls to the side and stands up with one or both hands on the floor to start to rise but does not touch legs 6=Stands up without rolling over or using hands on legs or floor

Full Analysis population: All patients in the Randomized Population who received at least 1 dose of study drug and provided at least 1 valid post Baseline NSAA efficacy assessment.

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 52

End point values	Dose 1	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	38		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change From Baseline in Time to Stand From Supine	-0.0389 (± 0.06728)	0.0459 (± 0.06171)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 4-stair Climb

End point title	Change From Baseline in 4-stair Climb

End point description:

To assess the change from baseline to Week 52 on the 4-Stair Climb. For timed function tests (TFTs) , the time will be set to 12 seconds and the speed to 0 if the TFT assessment meets the following TFT grading criteria. Grade of 1(from a 6-point scale)1=Unable to climb 4 standard stairs(no time recorded) 2=Climbs 4 standard stairs “marking time”(climbs one foot at a time, with both feet on a step before moving to next step), uses both arms on one or both handrails or uses 1 handrail and the other arm pushes on the leg 3=Climbs 4 standard stairs “marking time”, using one arm on one handrail or one hand pushing on leg or body 4=Climbs 4 standard stairs “marking time”, not needing handrail and not using hands to push on leg 5=Climbs 4 standard stairs alternating feet, needs handrail/s for support or uses arms to push on the leg or body 6=Climbs 4 standard stairs alternating feet, not needing handrail support or using arm to push
on the leg

Full Analysis population

End point type	Secondary

End point timeframe:

Baseline (Day 1) to Week 52

End point values	Dose 1	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	38		
Units: score on a scale				
arithmetic mean (standard deviation)	-0.0220 (± 0.08920)	-0.0392 (± 0.07352)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and Tolerability Measured by Number of Treatment- Emergent Adverse Events (TEAEs) and Serious Adverse

End point title	Safety and Tolerability Measured by Number of Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse

End point description:

Safety population: All patients who received at least 1 dose of study drug, with patients analyzed based on the actual study treatment received. This included the set of patients who were assigned the same treatment as their randomized sibling.

Adverse events that occurred from the time of the administration of the first dose of investigational product (IP) through
the end of the safety follow-up were considered treatment-emergent AEs (TEAEs).

Treatment-Related TEAEs (TRT-Related TATEs)

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Dose 1	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	43		
Units: participants				
Treatment Emergent Adverse Event (TEAEs)	85	41		
Related Treatment Emergent Adverse Event (TEAEs)	61	14		
Serious TEAE	1	1		
Serious Related TEAEs	0	0		
TEAEs Leading to Study Discontinuation	1	0		
TRT-Related TEAEs Leading to Study	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 52

Adverse event reporting additional description:

A treatment-emergent Adverse Events (TEAE) is any Adverse Events that newly appeared, increased in frequency or worsened in severity following initiation of study drug administration. Subjects with more than one AE of the same system organ class (SOC) / preferred term (PT) were counted only once for that SOC / PT.

Safety population

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	Dose 1

Reporting group description:

Edasalonexent 100 mg/kg/day. Capsules taken by mouth three times per day.

Reporting group title	Placebo

Reporting group description:

Matching placebo

Serious adverse events	Dose 1	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 88 (1.14%)	1 / 43 (2.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 43 (2.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus A			
subjects affected / exposed	1 / 88 (1.14%)	0 / 43 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Dose 1	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 88 (96.59%)	41 / 43 (95.35%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 88 (6.82%)	0 / 43 (0.00%)	
occurrences (all)	6	0	
Influenza like illness A			
subjects affected / exposed	0 / 88 (0.00%)	5 / 43 (11.63%)	
occurrences (all)	0	6	
Non-cardiac chest pain			
subjects affected / exposed	3 / 88 (3.41%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Pyrexia			
subjects affected / exposed	17 / 88 (19.32%)	9 / 43 (20.93%)	
occurrences (all)	18	14	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 88 (14.77%)	11 / 43 (25.58%)	
occurrences (all)	19	15	
Rhinorrhoea			
subjects affected / exposed	3 / 88 (3.41%)	5 / 43 (11.63%)	
occurrences (all)	4	8	
Epistaxis			
subjects affected / exposed	6 / 88 (6.82%)	1 / 43 (2.33%)	
occurrences (all)	10	3	
Oropharyngeal pain			
subjects affected / exposed	4 / 88 (4.55%)	1 / 43 (2.33%)	
occurrences (all)	5	1	
Sinus congestion			
subjects affected / exposed	3 / 88 (3.41%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Psychiatric disorders			
Attention deficit hyperactivity disorder			

subjects affected / exposed	2 / 88 (2.27%)	1 / 43 (2.33%)	
occurrences (all)	2	1	
Investigations			
Weight increased			
subjects affected / exposed	1 / 88 (1.14%)	2 / 43 (4.65%)	
occurrences (all)	1	2	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	2 / 88 (2.27%)	1 / 43 (2.33%)	
occurrences (all)	2	1	
Contusion			
subjects affected / exposed	6 / 88 (6.82%)	2 / 43 (4.65%)	
occurrences (all)	11	2	
Fall			
subjects affected / exposed	14 / 88 (15.91%)	4 / 43 (9.30%)	
occurrences (all)	20	5	
Ligament sprain			
subjects affected / exposed	3 / 88 (3.41%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 88 (3.41%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Headache			
subjects affected / exposed	12 / 88 (13.64%)	8 / 43 (18.60%)	
occurrences (all)	15	10	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	3 / 88 (3.41%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	4 / 88 (4.55%)	1 / 43 (2.33%)	
occurrences (all)	4	1	
Abdominal pain			

subjects affected / exposed	7 / 88 (7.95%)	1 / 43 (2.33%)	
occurrences (all)	14	1	
Abdominal pain upper			
subjects affected / exposed	15 / 88 (17.05%)	9 / 43 (20.93%)	
occurrences (all)	22	15	
Constipation			
subjects affected / exposed	6 / 88 (6.82%)	3 / 43 (6.98%)	
occurrences (all)	7	3	
Dental caries			
subjects affected / exposed	2 / 88 (2.27%)	1 / 43 (2.33%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	54 / 88 (61.36%)	12 / 43 (27.91%)	
occurrences (all)	94	20	
Faeces soft			
subjects affected / exposed	2 / 88 (2.27%)	1 / 43 (2.33%)	
occurrences (all)	3	1	
Nausea			
subjects affected / exposed	7 / 88 (7.95%)	5 / 43 (11.63%)	
occurrences (all)	8	5	
Toothache			
subjects affected / exposed	3 / 88 (3.41%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Vomiting			
subjects affected / exposed	29 / 88 (32.95%)	11 / 43 (25.58%)	
occurrences (all)	57	18	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	20 / 88 (22.73%)	2 / 43 (4.65%)	
occurrences (all)	25	2	
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	2 / 88 (2.27%)	2 / 43 (4.65%)	
occurrences (all)	2	4	
Pollakiuria			

subjects affected / exposed	3 / 88 (3.41%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 88 (1.14%)	2 / 43 (4.65%)	
occurrences (all)	1	2	
Muscle spasms			
subjects affected / exposed	10 / 88 (11.36%)	1 / 43 (2.33%)	
occurrences (all)	11	1	
Pain in extremity			
subjects affected / exposed	6 / 88 (6.82%)	5 / 43 (11.63%)	
occurrences (all)	11	7	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	18 / 88 (20.45%)	5 / 43 (11.63%)	
occurrences (all)	26	5	
Conjunctivitis			
subjects affected / exposed	2 / 88 (2.27%)	1 / 43 (2.33%)	
occurrences (all)	2	1	
Ear infection			
subjects affected / exposed	7 / 88 (7.95%)	5 / 43 (11.63%)	
occurrences (all)	9	5	
Gastroenteritis			
subjects affected / exposed	3 / 88 (3.41%)	2 / 43 (4.65%)	
occurrences (all)	3	2	
Gastroenteritis viral			
subjects affected / exposed	3 / 88 (3.41%)	2 / 43 (4.65%)	
occurrences (all)	3	3	
Impetigo			
subjects affected / exposed	3 / 88 (3.41%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Influenza			
subjects affected / exposed	10 / 88 (11.36%)	2 / 43 (4.65%)	
occurrences (all)	10	3	
Lower respiratory tract infection			

subjects affected / exposed	2 / 88 (2.27%)	2 / 43 (4.65%)	
occurrences (all)	2	2	
Nasopharyngitis			
subjects affected / exposed	19 / 88 (21.59%)	9 / 43 (20.93%)	
occurrences (all)	28	13	
Pharyngitis streptococcal			
subjects affected / exposed	4 / 88 (4.55%)	4 / 43 (9.30%)	
occurrences (all)	4	4	
Tonsillitis			
subjects affected / exposed	3 / 88 (3.41%)	0 / 43 (0.00%)	
occurrences (all)	3	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 88 (6.82%)	2 / 43 (4.65%)	
occurrences (all)	7	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 April 2020	The amendment included the following key changes in response to the COVID-19 pandemic: • As patients may not have been able to come on-site for visits or for a reduced amount of time, modifications were made to the original study procedures and schedule of assessments to reduce the patient's risk or exposure to COVID-19 for Week 39 and Week 52 study visits. The modifications included: - Allowance for the Week 52 visit to be conducted out of the visit window (but in no case should the projected target date have been changed by more than 2 months). - Ability to perform study procedures either on site or remotely by using alternative approaches to collect study assessments. - Remote assessment for AEs and concomitant medications, as the top priority was safety. - Ability to defer other safety assessments, including physical examinations, chemistry and hematology labs and urinalysis for 6-month intervals if not feasible, based on the safety profile of edasalonexent to date and the consideration that all patients in this study had been on study drug for 6 months. - Allowance for drug dispensation to take place according to local site procedures, including secured, temperature-controlled shipments to the patients' homes • A prioritized list of assessments has been included in Appendix of the protocol. • Clarification that post the COVID-19 pandemic, clinical monitoring may resume at amore intense pace to clean all data accumulated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported