Clinical trial results:
A Phase 2 Open-label Study to Assess the Safety, Tolerability, and Efficacy of Viltolarsen in Ambulant and Non-Ambulant Boys with Duchenne Muscular Dystrophy (DMD) Compared to Natural History Controls

Summary

EudraCT number	2020-003653-30
Trial protocol	IT ES
Global end of trial date	13 July 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	NS-065/NCNP-01-211

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04956289
WHO universal trial number (UTN)	-
Other trial identifiers	US IND: 127474

Notes:

Sponsors

Sponsor organisation name	NS Pharma, Inc.
Sponsor organisation address	140 East Ridgewood Ave, Suite 280S Paramus, NJ , NJ, United States, NJ 07652
Public contact	Clinical Trial Management, Medpace, 001 51357999111270, regsubmissions@medpace.com
Scientific contact	Clinical Trial Management, Medpace, 001 51357999111270, regsubmissions@medpace.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002853-PIP01-20
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	26 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 July 2023
Global end of trial reached?	Yes
Global end of trial date	13 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of viltolarsen administered intravenously (IV) at weekly doses of 80 mg/kg in ambulant and non ambulant boys >= 8 years of age with DMD

Protection of trial subjects:

All considerations regarding the protection of human subjects were carried out in accordance with the protocol, GCP, ICH Guidelines, the ethical principles that have their origin in the Declaration of Helsinki, and all applicable regulatory requirements. The investigator (according to applicable regulatory requirements) or a person designated by the investigator and under the investigator's responsibility fully informed patients of all pertinent aspects of the clinical trial.

Background therapy:

Not applicable.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	05 April 2021
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	Spain: 1
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	China: 4
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Türkiye: 5
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	20
EEA total number of subjects	4

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)	13
Adolescents (12-17 years)	4
Adults (18-64 years)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Twenty-one (21) patients were screened. Five patients were screen failed (4 patients due to reasons related to COVID-19 and 1 patient due to failure to satisfy exclusion criterion 1) and were rescreened and dosed. One patient was screen failure due to failure to satisfy exclusion criterion 5 and was not dosed. Twenty (20) patients were dosed.

Pre-assignment

Screening details:

Ambulant and non-ambulant boys ≥8 years of age with a confirmed diagnosis of Duchenne Muscular Dystrophy (DMD), who had a Brooke scale rating of 3 or better OR an upright Forced Vital Capacity (FVC) 30% or greater at Screening, on a stable dose of glucocorticoid (GC) or were not treated with GC for at least 3 months prior to the first dose.

Period 1

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

Blinding implementation details:

Not applicable.

Arms

Arm title	Viltolarsen 80 mg/kg

Arm description:

Patients received IV infusions of viltolarsen injection administered once weekly over a 48-week period. Patients were dosed at 80 mg/kg/week.

Arm type	Experimental
Investigational medicinal product name	Viltolarsen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Viltolarsen injection 250 mg aqueous infusion was supplied as a 5 mL glass vial containing 50 mg/mL of drug substance solution in saline.
Patients received IV infusions of viltolarsen injection administered once weekly over a 48-week period. Patients were dosed at 80 mg/kg/week.

Viltolarsen is a novel antisense oligonucleotide for the treatment of DMD. Viltolarsen is designed to interact with the dystrophin gene ribonucleic acid (RNA) and alter the exon/intron splicing patterns. The mechanism of action for viltolarsen is to bind to a specific sequence in or near exon 53 of the dystrophin pre-RNA transcript and block the exon/intron splicing of exon 53, leading to mature mRNA transcripts that lack exon 53. The loss of exon 53 restores the mRNA reading frame, thus converting a DMD (out-of-frame) deletion mutation to a Becker-like (in frame) deletion mutation.

Number of subjects in period 1	Viltolarsen 80 mg/kg
Started	20
Completed	20

Baseline characteristics

Reporting groups	
Reporting group title	Viltolarsen 80 mg/kg
Reporting group description:	
Patients received IV infusions of viltolarsen injection administered once weekly over a 48-week period. Patients were dosed at 80 mg/kg/week.	

Reporting group values	Viltolarsen 80 mg/kg	Total	
Number of subjects	20	20	
Age categorical			
Counts and percentages of patients in each analysis population are summarized based on all dosed patients. The modified Intent-to-Treat (mITT) Population consisted of all patients who received at least 1 dose of IP and had a baseline assessment and at least 1 post-baseline efficacy assessment. This was the analysis population for the evaluation of efficacy. The Safety Population consisted of all patients who received at least 1 dose of IP. This was the primary analysis population for the evaluation of safety.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	13	13	
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	3	3	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Counts and percentages of patients in each analysis population are summarized based on all dosed patients. The modified Intent-to-Treat (mITT) Population consisted of all patients who received at least 1 dose of IP and had a baseline assessment and at least 1 post-baseline efficacy assessment. This was the analysis population for the evaluation of efficacy. The Safety Population consisted of all patients who received at least 1 dose of IP. This was the primary analysis population for the evaluation of safety.			
Units: years			
arithmetic mean	12.8		
standard deviation	± 5.47	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	20	20	

Subject analysis sets	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Population consisted of all patients who received at least 1 dose of IP (Investigational	

Product). This was the primary analysis population for the evaluation of safety. It includes all patients treated with viltolarsen both ambulant (10) and non-ambulant (10).

Reporting group values	Safety Population		
Number of subjects	20		
Age categorical			
Counts and percentages of patients in each analysis population are summarized based on all dosed patients. The modified Intent-to-Treat (mITT) Population consisted of all patients who received at least 1 dose of IP and had a baseline assessment and at least 1 post-baseline efficacy assessment. This was the analysis population for the evaluation of efficacy. The Safety Population consisted of all patients who received at least 1 dose of IP. This was the primary analysis population for the evaluation of safety.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	13		
Adolescents (12-17 years)	4		
Adults (18-64 years)	3		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Counts and percentages of patients in each analysis population are summarized based on all dosed patients. The modified Intent-to-Treat (mITT) Population consisted of all patients who received at least 1 dose of IP and had a baseline assessment and at least 1 post-baseline efficacy assessment. This was the analysis population for the evaluation of efficacy. The Safety Population consisted of all patients who received at least 1 dose of IP. This was the primary analysis population for the evaluation of safety.			
Units: years			
arithmetic mean	12.8		
standard deviation	± 5.47		
Gender categorical			
Units: Subjects			
Female	0		
Male	20		

End points

End points reporting groups

Reporting group title	Viltolarsen 80 mg/kg

Reporting group description:

Patients received IV infusions of viltolarsen injection administered once weekly over a 48-week period. Patients were dosed at 80 mg/kg/week.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Population consisted of all patients who received at least 1 dose of IP (Investigational Product). This was the primary analysis population for the evaluation of safety. It includes all patients treated with viltolarsen both ambulant (10) and non-ambulant (10).

Primary: Treatment Related Adverse Events

End point title	Treatment Related Adverse Events[1]

End point description:

Number of participants with treatment related Adverse Events as assessed by CTCAE v4.03.

19 (95.0%) patients experienced a total of 66 TEAEs.
The maximum severity of TEAEs was mild for 7 (35.0%) patients and moderate in 12 (60.0%) patients. No patients experienced a severe TEAE.
2 (10.0%) patients experienced a TEAE which led to interruption in dosing. Most (17 [85.0%]) patients experienced TEAEs that were considered recovered or resolved. Two (10.0%) patients experienced TEAEs that were considered not recovered or resolved.
4 (20.0%) patients experienced a total of 4 IP-related TEAEs.
The maximum severity of IP related TEAEs was mild for 3 (15.0%) patients and moderate in 1 (5.0%) patient. No patients experienced a severe IP-related TEAE.
One (5.0%) patient experienced an IP-related TEAE that resulted in interruption in dosing. All IP related TEAEs were considered recovered or resolved.
Five (25.0%) patients experienced a total of 6 AESIs (Adverse event of special interest).

End point type	Primary

End point timeframe:

Baseline to up to 48 weeks of treatment.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for this endpoint. The information has been introduced in the section "Adverse Events".

End point values	Viltolarsen 80 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: patients	20			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
TEAEs were defined as any adverse events (AEs) that started on or after first dose of IP through 30 days after completion of study participation.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Safety Population
Reporting group description:	
The Safety Population consisted of all patients who received at least 1 dose of IP. This was the primary analysis population for the evaluation of safety. It includes all patients treated with viltolarsen both ambulant (10) and non-ambulant (10).	

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 20 (95.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Gait inability			

subjects affected / exposed occurrences (all) Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Respiratory, thoracic and mediastinal disorders Nasal congestion subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Investigations Protein urine subjects affected / exposed occurrences (all) Urine cytology abnormal subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Injury, poisoning and procedural complications Joint injury subjects affected / exposed occurrences (all) Contusion subjects affected / exposed occurrences (all) Ligament sprain subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Cardiac disorders Angina pectoris			

subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Tension headache subjects affected / exposed occurrences (all)	 4 / 20 (20.00%) 4 1 / 20 (5.00%) 2		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Food poisoning subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 8 2 / 20 (10.00%) 2 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Skin and subcutaneous tissue disorders Blister subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Renal and urinary disorders			

Haematuria subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 5		
Nephrolithiasis subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Back pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Myalgia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	6 / 20 (30.00%) 6		
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3		
Influenza subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Rhinitis subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Otitis media subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		
Pharyngitis			

subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 March 2022	The original Protocol (Version 1.0) was dated 21 January 2021. There was 1 global Amendment and 2 China-specific Amendments to the original Protocol. There were 4 Administrative Letters. This amendment was developed to specify the minimum number of ambulant patients to be enrolled in the study (a minimum of 8); to clarify a location of blood sampling during the investigational product infusion and post-infusion; to specify the blood draw volumes; to clarify time points when viltorasen levels in plasma will be assessed; and to add necessary clarifications to the home infusion option. In addition, the details of the Performance of Upper Limb 2.0 assessment were added, as was clarification of referencing the United States package insert for the purpose of expedited reporting to the United States Food and Drug Administration and the United States sites. The general considerations of planned statistical methods were updated. A section describing disclosure of data was added to the protocol appendices.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported