



Clinical trial results:

A Multicenter, Randomized, Parallel Group, Double Blind, Multiple Dose, Placebo Controlled Study to Assess the Efficacy and Safety of MNK-1411 in Male Subjects 4 to 8 Years of Age With Duchenne Muscular Dystrophy

Summary

EudraCT number	2017-004139-35
Trial protocol	ES BG IT
Global end of trial date	25 February 2020

Results information

Result version number	v1
This version publication date	06 September 2020
First version publication date	06 September 2020

Trial information

Trial identification

Sponsor protocol code	MNK14112096
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03400852
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mallinckrodt ARD LLC
Sponsor organisation address	1425 U.S. Route 206, Bedminster, NJ, United States, 07921
Public contact	Medical Information Call Center, Mallinckrodt ARD LLC, 1 1 800-844-2830 Ext 5, clinicaltrials@mnk.com
Scientific contact	Medical Information Call Center, Mallinckrodt ARD LLC, 1 1 800-844-2830 Ext 5, clinicaltrials@mnk.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 May 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 February 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to determine the effect of MNK-1411 on motor function in subjects with Duchenne Muscular Dystrophy (DMD). Information has been collected only from caretakers who are fluent in English, using the Pediatric Outcomes Data Collection Instrument (PODCI). The PODCI is a validated 86-question instrument completed by the parent or legal guardian of children 2 to 10 years of age to assess a variety of health outcome measures (Uzark et al, 2012). This study will only collect information for the PODCI domains of sports and physical functioning and transfer/basic mobility.

Protection of trial subjects:

The study was conducted in full compliance with applicable international, national and local regulatory requirements; US Food and Drug Administration (FDA) regulations including 21 CFR 314.106 and 312.120, (where applicable); and ICH guidelines for GCP and in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 July 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	Spain: 6
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Mexico: 18
Country: Number of subjects enrolled	Serbia: 2
Country: Number of subjects enrolled	Turkey: 3
Worldwide total number of subjects	44
EEA total number of subjects	10

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	44
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: -

Pre-assignment

Screening details:

After screening, 44 patients were randomized into blinded treatment groups at 16 sites in 8 countries.

Period 1

Period 1 title	Blinded Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Blinding implementation details:

Patients were randomized 2:1 to receive MNK-1411:placebo at the dose appropriate for their weight

Arms

Are arms mutually exclusive?	Yes
Arm title	MNK-1411

Arm description:

All patients who received any dose of MNK-1411 in Period 1

Arm type	Experimental
Investigational medicinal product name	Cosyntropin acetate
Investigational medicinal product code	MNK-1411
Other name	Tetracosactide Hexaacetate
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MNK-1411 suspension for subcutaneous injection

Arm title	Placebo
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Arm description:

All patients who received placebo in Period 1

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Matching placebo
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo suspension for subcutaneous administration

Number of subjects in period 1	MNK-1411	Placebo
Started	29	15
Completed	20	9
Not completed	9	6
Physician decision	-	1
Adverse event, non-fatal	1	1
Study terminated by sponsor	8	4

Period 2

Period 2 title	Open Label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

All patients entering open label period received MNK-1411

Arms

Arm title	MNK-1411
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Arm description:

All patients who entered the open label extension period receive MNK-1411

Arm type	Experimental
Investigational medicinal product name	Cosyntropin acetate
Investigational medicinal product code	MNK-1411
Other name	Tetracosactide Hexaacetate
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

MNK-1411 1 mg/ml [milligram(s)/milliliter] suspension for subcutaneous injection

Number of subjects in period 2 ^[1]	MNK-1411
Started	24
Completed	2
Not completed	22
Physician decision	1
Study terminated by sponsor	21

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Patients who chose to discontinue double-blind period prior to Week 24, entered OLE

period. Patients who did not enter OLE Period were followed-up to Week 28.

Baseline characteristics

Reporting groups

Reporting group title	MNK-1411
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Reporting group description:

All patients who received any dose of MNK-1411 in Period 1

Reporting group title	Placebo
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Reporting group description:

All patients who received placebo in Period 1

Reporting group values	MNK-1411	Placebo	Total
Number of subjects	29	15	44
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	29	15	44
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	5.7	6.3	
standard deviation	± 1.49	± 1.18	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	29	15	44

End points

End points reporting groups

Reporting group title	MNK-1411
Reporting group description: All patients who received any dose of MNK-1411 in Period 1	
Reporting group title	Placebo
Reporting group description: All patients who received placebo in Period 1	
Reporting group title	MNK-1411
Reporting group description: All patients who entered the open label extension period receive MNK-1411	

Primary: Time to Complete 10 Meter Walk/Run

End point title	Time to Complete 10 Meter Walk/Run ^[1]
End point description: 10 Meter Walk/Run is a motor function test to measure the functional capability in patients with DMD.	
End point type	Primary
End point timeframe: Baseline, Week 24	
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 analyses were performed to arrive at these descriptive statistics	

End point values	MNK-1411	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: Seconds				
median (full range (min-max))				
at Baseline	5.9 (4.7 to 22.3)	7.8 (3.9 to 13.0)		
at Week 24 (n=16,9)	5.4 (4.1 to 8.9)	8.7 (3.3 to 18.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: North Star Ambulatory Assessment (NSAA) Score

End point title	North Star Ambulatory Assessment (NSAA) Score
End point description: The NSAA is comprised of 17 items, each of which is graded using the standard scorecard. Each assessment is rated as 0 - unable to achieve independently, 1 - modified method but achieves goal independent of physical assistance from another, or 2 - normal with no obvious modification of activity. The subscale scores are summed for a total score ranging from 0 to 34. The higher the total score, the better the outcome.	

End point type	Secondary
End point timeframe:	
Baseline, Week 24	

End point values	MNK-1411	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: score on a scale				
arithmetic mean (standard deviation)				
at Baseline	17.9 (± 6.80)	17.1 (± 6.40)		
at Week 24 (n=17,9)	20.5 (± 7.94)	16.6 (± 8.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Climb 4 Standardized Stairs

End point title	Time to Climb 4 Standardized Stairs
End point description:	
Time to climb 4 standardized stairs is a motor performance test.	
End point type	Secondary
End point timeframe:	
Baseline, Week 24	

End point values	MNK-1411	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: Seconds				
arithmetic mean (standard deviation)				
at Baseline	8.528 (± 8.8832)	8.467 (± 4.3353)		
at Week 24 (n=15,9)	4.711 (± 2.4547)	15.087 (± 13.8414)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Stand from a Supine Position

End point title	Time to Stand from a Supine Position
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End point description:

Time to stand from a supine position is a motor function test to measure the functional capability in subjects with DMD.

End point type	Secondary
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End point timeframe:

Baseline, Week 24

End point values	MNK-1411	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	13		
Units: Seconds				
arithmetic mean (standard deviation)				
at Baseline	11.141 ($\pm$ 9.0756)	15.031 ($\pm$ 12.4518)		
at Week 24 (n=16,9)	7.645 ($\pm$ 4.9939)	24.889 ($\pm$ 26.4763)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative Muscle Testing Scores at Baseline

End point title	Quantitative Muscle Testing Scores at Baseline
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End point description:

Quantitative muscle testing measured strength-knee flexion and extension measured in Newtons, using a dynamometer.

End point type	Secondary
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End point timeframe:

at Baseline

End point values	MNK-1411	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	15		
Units: Newton				
arithmetic mean (standard deviation)				
Knee flexion	26.610 ($\pm$ 14.1697)	29.870 ($\pm$ 14.1697)		
Knee extension	28.987 ($\pm$ 16.2362)	26.643 ($\pm$ 15.2748)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative Muscle Testing Scores at Week 24

End point title	Quantitative Muscle Testing Scores at Week 24
End point description: Quantitative muscle testing measured strength-knee flexion and extension measured in Newtons, using a dynamometer.	
End point type	Secondary
End point timeframe: Week 24	

End point values	MNK-1411	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	9		
Units: Newtons				
arithmetic mean (standard deviation)				
Knee flexion	33.636 ($\pm$ 15.7832)	25.267 ($\pm$ 13.3471)		
Knee extension	26.610 ($\pm$ 14.1697)	29.870 ($\pm$ 15.1330)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Adverse Events in the Blinded Treatment Period

End point title	Summary of Adverse Events in the Blinded Treatment Period
End point description: Clinically significant changes in vital signs, height, weight, immunogenicity and laboratory assessments were reported as adverse events (AEs)	
End point type	Secondary
End point timeframe: within 28 weeks	

End point values	MNK-1411	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	15		
Units: Patients				
Number of patients exposed	29	15		
Number affected by serious adverse events	0	1		
Total number affected by non-serious AEs	22	15		
Total number of deaths (all causes)	0	0		

Number of deaths due to AEs	0	0		
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Statistical analyses

No statistical analyses for this end point

Secondary: Summary of AEs in the Open Label Extension Period

End point title	Summary of AEs in the Open Label Extension Period
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End point description:

Clinically significant changes in vital signs, height, weight, immunogenicity and laboratory assessments were reported as AEs

End point type	Secondary
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End point timeframe:

within 28 weeks

End point values	MNK-1411			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: Patients				
Number of patients exposed	24			
Number affected by SAEs	2			
Total number affected by non-serious AEs	11			
Total number of deaths (all causes)	0			
Number of deaths due to AEs	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

within 28 weeks

Adverse event reporting additional description:

Clinically significant changes in vital signs, height, weight, immunogenicity and laboratory assessment were reported as AEs

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	MNK-1411 (Blinded Treatment Period)
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Reporting group description:

All patients who received MNK-1411 during the blinded treatment period

Reporting group title	Placebo (Blinded Treatment Period)
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Reporting group description:

Patients who received placebo during the blinded treatment period

Reporting group title	MNK-1411 (Open Label Extension)
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Reporting group description:

Patients who received MNK-1411 during the open label extension period

Serious adverse events	MNK-1411 (Blinded Treatment Period)	Placebo (Blinded Treatment Period)	MNK-1411 (Open Label Extension)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	2 / 24 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MNK-1411 (Blinded Treatment Period)	Placebo (Blinded Treatment Period)	MNK-1411 (Open Label Extension)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 29 (75.86%)	15 / 15 (100.00%)	11 / 24 (45.83%)
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	2
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 29 (3.45%)	2 / 15 (13.33%)	0 / 24 (0.00%)
occurrences (all)	1	2	0
Fatigue			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Injection site bruising			
subjects affected / exposed	1 / 29 (3.45%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Injection site erythema			
subjects affected / exposed	4 / 29 (13.79%)	1 / 15 (6.67%)	1 / 24 (4.17%)
occurrences (all)	4	1	1
Injection site haematoma			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0

Injection site induration subjects affected / exposed occurrences (all)	4 / 29 (13.79%) 4	1 / 15 (6.67%) 1	2 / 24 (8.33%) 2
Injection site irritation subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	1 / 15 (6.67%) 1	0 / 24 (0.00%) 0
Injection site mass subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	3 / 15 (20.00%) 3	1 / 24 (4.17%) 1
Injection site pain subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 2	1 / 15 (6.67%) 1	0 / 24 (0.00%) 0
Injection site swelling subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 15 (0.00%) 0	0 / 24 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 15 (13.33%) 2	1 / 24 (4.17%) 1
Swelling face subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	0 / 15 (0.00%) 0	0 / 24 (0.00%) 0
Immune system disorders Allergy to arthropod bite subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	1 / 15 (6.67%) 2	1 / 24 (4.17%) 2
Respiratory, thoracic and mediastinal disorders Bronchial hyperreactivity subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	1 / 15 (6.67%) 1	0 / 24 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	2 / 29 (6.90%) 3	2 / 15 (13.33%) 2	0 / 24 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	1 / 15 (6.67%) 1	0 / 24 (0.00%) 0
Asthma			

subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 15 (0.00%) 0	1 / 24 (4.17%) 1
Psychiatric disorders			
Affect lability			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 29 (3.45%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Mood swings			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Separation anxiety disorder			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Investigations			
Weight increased			
subjects affected / exposed	7 / 29 (24.14%)	0 / 15 (0.00%)	3 / 24 (12.50%)
occurrences (all)	9	0	3
Nerve stimulation test abnormal			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Congestive cardiomyopathy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	2
Nervous system disorders			
Headache			

subjects affected / exposed	2 / 29 (6.90%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Motor dysfunction			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	2 / 29 (6.90%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Aphthous ulcer			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	2	0	1
Food poisoning			
subjects affected / exposed	1 / 29 (3.45%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	1	1	0
Irritable bowel syndrome			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Hirsutism			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Hypertrichosis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Swelling face			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Lipohypertrophy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Glycosuria			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	3
Endocrine disorders			
Cushing's syndrome			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Cushingoid			
subjects affected / exposed	2 / 29 (6.90%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			

Muscle spasms			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 29 (0.00%)	3 / 15 (20.00%)	1 / 24 (4.17%)
occurrences (all)	0	4	1
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	1 / 15 (6.67%)	1 / 24 (4.17%)
occurrences (all)	2	1	1
Gastroenteritis viral			
subjects affected / exposed	2 / 29 (6.90%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Enterobiasis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Otitis media acute			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 15 (13.33%)	0 / 24 (0.00%)
occurrences (all)	0	2	0
Pharyngotonsillitis			

subjects affected / exposed	3 / 29 (10.34%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	3	0	0
Scarlet fever			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Tonsillitis bacterial			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	2 / 15 (13.33%)	1 / 24 (4.17%)
occurrences (all)	1	2	1
Urinary tract infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 15 (6.67%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Viral pharyngitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperglycaemia			

subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Hyperphagia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
subjects affected / exposed	1 / 29 (3.45%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	1	0	1
Hypokalaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 15 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 November 2017	Protocol Amendment 1 was developed to address issues raised by the central institutional review board including adding a study drug taper followed by a cosyntropin stimulation test and clarifying parent and/or legal guardian consent. Additional minor changes that do not impact study conduct or subject safety were also made.
22 August 2018	Protocol Amendment 2 was developed to address the following considerations: - In a randomized, double-blind, placebo controlled crossover study in patients ages 5 to 8 with Duchenne muscular dystrophy Beenakker et al, 2005 utilized a 2 month washout period between treatment periods with prednisone and placebo and this washout period appeared to be effective. Subsequently a Medical Advisory Board evaluated the current study design and based on their clinical experience recommended allowing the enrollment of subjects who have not received a therapeutic dose of corticosteroids within 2 months prior to the start of the study. - Subjects with asthma are excluded from the study. Therefore, the concomitant use of inhaled corticosteroids (whose approved indication is for asthma) should not be permitted.
23 May 2019	To accommodate subject needs, Protocol Amendment 3 was developed primarily to extend the Open Label Extension Period beyond Week 52 (to continue until the subject chooses to discontinue treatment, the investigator feels that treatment is no longer indicated, MNK-1411 is approved and marketed, or the sponsor ceases development of this compound for Duchenne Muscular Dystrophy [DMD]). Open label visits will continue every 12 weeks, with dispensing of study drug every 12 weeks. Along with this change, text has been added stating that if a subject requires a switch in dose during the Open Label Extension Period (eg, switch to low dose due to being unable to tolerate high dose, or switch to high dose based on increased weight [eg, as subject grows with age]), the investigator should consult with the medical monitor. Since subjects will be participating in the study longer, measurements of height have been added to all study visits. Additional major protocol changes are summarized below: -To accommodate the needs of study sites in Israel, the combination of Sunday and Wednesday has been added as possible visit and/or dosage administration days. -Text has been added specifying that subjects who have a hypersensitivity reaction to the study drug are not required to undergo the 2-week taper, or standard cosyntropin stimulation test (250 µg) at the follow-up visit. -Varicella zoster testing has been added along with an inclusion criterion (Inclusion criterion 6) requiring subjects to test positive prior to study entry (since such infections may be serious in patients who are immunosuppressed). -Pharmacokinetic analysis text has been corrected. -Additional guidance on the administration of motor tests has been provided, along with modification of Exclusion criterion 7 to require that subjects be able to complete the 10 Meter Walk/Run test in 10 seconds or less at the Screening and Baseline Visits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
25 February 2020	The trial was permanently discontinued because of slow enrollment.	-

Notes:

Limitations and caveats

None reported