Clinical trial results:
A Multicenter Open-Label Study on the Safety and Efficacy of Deflazacort (Emflaza) in Subjects With Limb-Girdle Muscular Dystrophy 2I (LGMD2I)

Summary

EudraCT number	2018-004740-36
Trial protocol	DE FR DK
Global end of trial date	01 January 2021

Results information

Result version number	v1 (current)
This version publication date	01 August 2022
First version publication date	01 August 2022

Trial information

Trial identification

Sponsor protocol code	PTCEMF-GD-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03783923
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	PTC Therapeutics, Inc.
Sponsor organisation address	100 Corporate Court, South Plainfield, United States, NJ 07080
Public contact	Medical Information, PTC Therapeutics, Inc., +011 44 1-866-562-4620, medinfo@ptcbio.com
Scientific contact	Medical Information, PTC Therapeutics International Limited, +353 19068700, medinfo@ptcbio.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	01 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 January 2021
Global end of trial reached?	Yes
Global end of trial date	01 January 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of deflazacort as measured by muscle function in participants with LGMD2I.

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Harmonized Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	11
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	10
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants enrolled under protocol v3.0 were 1:1 randomized to get placebo or deflazacort. After protocol v4.0, the study became an open-label study and all participants received deflazacort.
Per planned analysis, participants who took at least 1 dose of deflazacort were pooled in the safety and efficacy summaries.

Period 1

Period 1 title	Placebo-Controlled Period (26 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Deflazacort

Arm description:

Participants received deflazacort tablets, administered orally once daily at a target dose of 0.6 milligrams (mg)/kilograms (kg)/day for 26 weeks in placebo-controlled period and for 26 weeks in open-label extension period.

Arm type	Experimental
Investigational medicinal product name	Deflazacort
Investigational medicinal product code	
Other name	Emflaza®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

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

Arm title	Placebo

Arm description:

Participants received placebo matched to deflazacort tablets, administered orally once daily for 26 weeks in placebo-controlled period. Participants were then transitioned to receive deflazacort tablets, administered orally once daily at a target dose of 0.6 mg/kg/day for 26 weeks in open-label extension period.

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

Dosage and administration details:

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

Number of subjects in period 1	Deflazacort	Placebo
Started	5	6
Safety population	5	2
Completed	1	2
Not completed	4	4
Consent withdrawn by subject	-	2
Adverse event, non-fatal	1	-
Study Terminated	3	2

Period 2

Period 2 title	Open-Label Extension (26 Weeks)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Deflazacort

Arm description:

Participants received deflazacort tablets, administered orally once daily at a target dose of 0.6 milligrams (mg)/kilograms (kg)/day for 26 weeks in placebo-controlled period and for 26 weeks in open-label extension period.

Arm type	Experimental
Investigational medicinal product name	Deflazacort
Investigational medicinal product code	
Other name	Emflaza®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

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

Arm title	Placebo

Arm description:

Participants received placebo matched to deflazacort tablets, administered orally once daily for 26 weeks in placebo-controlled period. Participants were then transitioned to receive deflazacort tablets, administered orally once daily at a target dose of 0.6 mg/kg/day for 26 weeks in open-label extension period.

Arm type	Placebo
Investigational medicinal product name	Deflazacort
Investigational medicinal product code	
Other name	Emflaza®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

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

Number of subjects in period 2	Deflazacort	Placebo
Started	1	2
Completed	0	0
Not completed	1	2
Consent withdrawn by subject	1	1
Study Terminated	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Deflazacort
Reporting group description:	
Participants received deflazacort tablets, administered orally once daily at a target dose of 0.6 milligrams (mg)/kilograms (kg)/day for 26 weeks in placebo-controlled period and for 26 weeks in open-label extension period.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo matched to deflazacort tablets, administered orally once daily for 26 weeks in placebo-controlled period. Participants were then transitioned to receive deflazacort tablets, administered orally once daily at a target dose of 0.6 mg/kg/day for 26 weeks in open-label extension period.	

Reporting group values	Deflazacort	Placebo	Total
Number of subjects	5	6	11
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	5	5	10
>=65 years	0	1	1
Sex: Female, Male Units: participants			
Female	4	4	8
Male	1	2	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	5	6	11
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Deflazacort

Reporting group description:

Participants received deflazacort tablets, administered orally once daily at a target dose of 0.6 milligrams (mg)/kilograms (kg)/day for 26 weeks in placebo-controlled period and for 26 weeks in open-label extension period.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to deflazacort tablets, administered orally once daily for 26 weeks in placebo-controlled period. Participants were then transitioned to receive deflazacort tablets, administered orally once daily at a target dose of 0.6 mg/kg/day for 26 weeks in open-label extension period.

Reporting group title	Deflazacort

Reporting group description:

Participants received deflazacort tablets, administered orally once daily at a target dose of 0.6 milligrams (mg)/kilograms (kg)/day for 26 weeks in placebo-controlled period and for 26 weeks in open-label extension period.

Reporting group title	Placebo

Reporting group description:

Participants received placebo matched to deflazacort tablets, administered orally once daily for 26 weeks in placebo-controlled period. Participants were then transitioned to receive deflazacort tablets, administered orally once daily at a target dose of 0.6 mg/kg/day for 26 weeks in open-label extension period.

Subject analysis set title	Deflazacort
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received deflazacort tablets, administered orally once daily at a target dose of 0.6 mg/kg/day.

Primary: Change From Baseline in Time to Climb 4 Stairs After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Time to Climb 4 Stairs After 26 Weeks of Treatment With Deflazacort[1]

End point description:

Safety population included all enrolled participants who received at least 1 dose of deflazacort. Here, 'n' = participants evaluable at specified timepoint. 99999 = Single participant was analyzed; hence, standard deviation (SD) could not be calculated.

End point type	Primary

End point timeframe:

Baseline, Week 26

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: The endpoint is descriptive in nature.

End point values	Deflazacort			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n = 7)	5.476 (± 2.0178)			

Change at Week 26 (n = 1)	-0.200 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity (FVC) After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Forced Vital Capacity (FVC) After 26 Weeks of Treatment With Deflazacort[2]

End point description:

Due to early termination of the study and missing efficacy assessment data due to missed visits related to COVID-19, data was not collected or analyzed for this secondary efficacy endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for specified arm only.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: liters				
arithmetic mean (standard deviation)	()			

Notes:

[3] - Due to early termination of study, data was not collected or analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 2-Minute Walk Test After 26 Weeks of Treatment of Deflazacort

End point title	Change From Baseline in 2-Minute Walk Test After 26 Weeks of Treatment of Deflazacort

End point description:

Safety population included all enrolled participants who received at least 1 dose of deflazacort. Here, 'n' = participants evaluable at specified timepoint. 99999 = Single participant was analyzed; hence, SD could not be calculated.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Deflazacort			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: meters				
arithmetic mean (standard deviation)				
Baseline (n = 7)	135.4 (± 26.75)			
Change at Week 26 (n = 1)	2.0 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to up and go After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Time to up and go After 26 Weeks of Treatment With Deflazacort

End point description:

Safety population included all enrolled participants who received at least 1 dose of deflazacort. Here, 'n' = participants evaluable at specified timepoint. 99999 = Single participant was analyzed; hence, SD could not be calculated.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Deflazacort			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n = 7)	11.93 (± 4.743)			
Change at Week 26 (n = 1)	9.70 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Descend 4 Stairs After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Time to Descend 4 Stairs After 26 Weeks of Treatment With Deflazacort

End point description:

Safety population included all enrolled participants who received at least 1 dose of deflazacort. Here, 'n' = participants evaluable at specified timepoint. 99999 = Single participant was analyzed; hence, SD could not be calculated.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Deflazacort			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n = 7)	3.66 (± 1.707)			
Change at Week 26 (n =1)	0.10 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Run/Walk 10 Meters After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Time to Run/Walk 10 Meters After 26 Weeks of Treatment With Deflazacort

End point description:

Safety population included all enrolled participants who received at least 1 dose of deflazacort. Here, 'n' = participants evaluable at specified timepoint. 99999 = Single participant was analyzed; hence, SD could not be calculated.

End point type	Secondary

End point timeframe:

Baseline, Week 26

End point values	Deflazacort			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: seconds				
arithmetic mean (standard deviation)				
Baseline (n = 7)	8.53 (± 1.897)			
Change at Week 26 (n = 1)	-0.40 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Maximal Inspiratory Pressure (MIP) and

Maximal Expiratory Pressure (MEP) After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Maximal Inspiratory Pressure (MIP) and Maximal Expiratory Pressure (MEP) After 26 Weeks of Treatment With Deflazacort[4]

End point description:

Due to early termination of the study and missing efficacy assessment data due to missed visits related to COVID-19, data was not collected or analyzed for this secondary efficacy endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is descriptive in nature.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: centimeters				
arithmetic mean (standard deviation)	()			

Notes:

[5] - Due to early termination of the study, data was not collected or analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Hand-Held Myometry After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Hand-Held Myometry After 26 Weeks of Treatment With Deflazacort[6]

End point description:

Due to early termination of the study and missing efficacy assessment data due to missed visits related to COVID-19, data was not collected or analyzed for this secondary efficacy endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is descriptive in nature.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: newtons				
arithmetic mean (standard deviation)	()			

Notes:

[7] - Due to early termination of the study, data was not collected or analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Global T2 Relaxation Time of Selected Upper and Lower Limb Muscles After 26 Weeks of Treatment With Deflazacort

End point title	Change From Baseline in Global T2 Relaxation Time of Selected Upper and Lower Limb Muscles After 26 Weeks of Treatment With Deflazacort[8]

End point description:

Due to early termination of the study and missing efficacy assessment data due to missed visits related to COVID-19, data was not collected or analyzed for this secondary efficacy endpoint.

End point type	Secondary

End point timeframe:

Baseline, Week 26

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is descriptive in nature.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	0[9]			
Units: seconds				
arithmetic mean (standard deviation)	()			

Notes:

[9] - Due to early termination of the study, data was not collected or analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)

End point description:

An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. AEs included both SAEs and non-serious AEs. A summary of other non-serious AEs and all SAEs, regardless of causality is located in the 'Reported AE section'. AEs were summarized separately for Stage 1 and for the overall ataluren experience. Safety population included all enrolled participants who received at least 1 dose of deflazacort. Per planned analysis, participants who took at least 1 dose of deflazacort were pooled in the safety summaries. The participants who received only placebo during the study were not included for safety analysis.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	Deflazacort			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Curve From Time Zero to t (AUC0-t) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort

End point title	Area Under the Concentration Curve From Time Zero to t (AUC0-t) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort[10]

End point description:

The pharmacokinetic (PK) population included all enrolled participants who received at least 1 dose of deflazacort and had at least one PK profile. Here, 'n' = participants evaluable for specified category. 99999 = Due to concentration below the limit of quantitation (BLQ) of 0.50 ng/mL, data not calculated.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, and 6 hours post-dose at Baseline and Week 13

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for specified arm only.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: nanograms (ng)*hour (hr)/milliliter (mL)				
arithmetic mean (standard deviation)				
21-desacetyl deflazacort: Baseline (n=4)	401.1 (± 139.62)			
21-desacetyl deflazacort: Week 13 (n=2)	365.6 (± 99999)			
6β-hydroxy-21-desacetyl deflazacort: Week 1 (n=4)	418.2 (± 58.569)			
6β-hydroxy-21-desacetyl deflazacort: Week 13 (n=2)	515.3 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Curve From Time Zero to Infinity (AUC0-inf) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort

End point title	Area Under the Concentration Curve From Time Zero to Infinity (AUC0-inf) of 21-desacetyl deflazacort and 6β-hydroxy-21-

	desacetyl deflazacort[11]

End point description:

The PK population included all enrolled participants who received at least 1 dose of deflazacort and had at least one PK profile. Here, 'n' = participants evaluable for specified category. 99999 = No participant was analyzed; hence, data not available.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, and 6 hours post-dose at Baseline and Week 13

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for specified arm only.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng*hr/mL				
arithmetic mean (standard deviation)				
21-desacetyl deflazacort: Baseline (n=4)	423.6 (± 150.16)			
21-desacetyl deflazacort: Week 13 (n=0)	99999 (± 99999)			
6β-hydroxy-21-desacetyl deflazacort: Week 1 (n=3)	520.3 (± 31.508)			
6β-hydroxy-21-desacetyl deflazacort: Week 13 (n=0)	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort

End point title	Maximum Observed Plasma Concentration (Cmax) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort[12]

End point description:

The PK population included all enrolled participants who received at least 1 dose of deflazacort and had at least one PK profile. Here, 'n' = participants evaluable for specified category. 99999 = Due to concentration BLQ of 0.50 ng/mL, data not calculated.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, and 6 hours post-dose at Baseline and Week 13

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for specified arm only.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng/mL				
arithmetic mean (standard deviation)				
21-desacetyl deflazacort: Baseline (n=4)	184.8 (± 49.054)			
21-desacetyl deflazacort: Week 13 (n=2)	171.0 (± 99999)			
6β-hydroxy-21-desacetyl deflazacort: Week 1 (n=4)	135.8 (± 29.205)			
6β-hydroxy-21-desacetyl deflazacort: Week 13 (n=2)	162.0 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Cmax (Tmax) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort

End point title	Time to Reach Cmax (Tmax) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort[13]

End point description:

The PK population included all enrolled participants who received at least 1 dose of deflazacort and had at least one PK profile. Here, 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, and 6 hours post-dose at Baseline and Week 13

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for specified arm only.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hr				
median (full range (min-max))				
21-desacetyl deflazacort: Baseline (n=4)	0.992 (0.50 to 1.00)			
21-desacetyl deflazacort: Week 13 (n=2)	0.525 (0.50 to 0.55)			
6β-hydroxy-21-desacetyl deflazacort: Week 1 (n=4)	1.000 (1.00 to 1.90)			
6β-hydroxy-21-desacetyl deflazacort: Week 13 (n=2)	1.550 (1.10 to 2.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Half-Life (t1/2) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort

End point title	Half-Life (t1/2) of 21-desacetyl deflazacort and 6β-hydroxy-21-desacetyl deflazacort[14]

End point description:

The PK population included all enrolled participants who received at least 1 dose of deflazacort and had at least one PK profile. Here, 'Number analyzed' = participants evaluable for specified category. 99999 = Due to concentration BLQ of 0.50 ng/mL, data not calculated. 9999 = Single participant was analyzed; hence, SD could not be calculated.

End point type	Secondary

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, and 6 hours post-dose at Baseline and Week 13

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is reporting statistics for specified arm only.

End point values	Deflazacort			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: hr				
arithmetic mean (standard deviation)				
21-desacetyl deflazacort: Baseline (n=4)	1.174 (± 0.0849)			
21-desacetyl deflazacort: Week 13 (n=2)	1.235 (± 99999)			
6β-hydroxy-21-desacetyl deflazacort: Week 1 (n=3)	2.358 (± 0.5825)			
6β-hydroxy-21-desacetyl deflazacort: Week 13 (n=1)	1.95 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to Week 52

Adverse event reporting additional description:

Safety population included all enrolled participants who received at least 1 dose of deflazacort. Per planned analysis, participants who took at least 1 dose of deflazacort were pooled in the safety summaries. Participants who received only placebo (not deflazacort) during the study were not monitored for safety assessments per planned analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Deflazacort

Reporting group description:

Participants received deflazacort tablets, administered orally once daily at a target dose of 0.6 mg/kg/day.

Serious adverse events	Deflazacort		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Deflazacort		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Amenorrhoea	Additional description: This is a gender-specific AE. Only female participants were at risk.		
subjects affected / exposed[1]	1 / 5 (20.00%)		
occurrences (all)	1		

Menstruation irregular	Additional description: This is a gender-specific AE. Only female participants were at risk.		
subjects affected / exposed[2]	1 / 5 (20.00%)		
occurrences (all)	1		
Psychiatric disorders			
Apathy			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Investigations			
Weight increased			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Skin laceration			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Post-traumatic pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Spinal compression fracture			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all) Hypoaesthesia subjects affected / exposed occurrences (all) Tension headache subjects affected / exposed occurrences (all) Visual field defect subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 1 1 / 7 (14.29%) 2		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Abnormal hair growth subjects affected / exposed occurrences (all) Hirsutism subjects affected / exposed occurrences (all)	 2 / 7 (28.57%) 2 1 / 7 (14.29%) 1 1 / 7 (14.29%) 1		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 1		
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all)	 1 / 7 (14.29%) 1		
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Muscle tightness			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	2		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This is a gender-specific AE. Only female participants were at risk.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This is a gender-specific AE. Only female participants were at risk.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2019	The overall reasons for this amendment were to include DEXA as an additional safety assessment in participants with LGMD2I. In addition, several editorial changes were made to clarify and correct the text.
26 September 2019	The overall reasons for this amendment were to address regulatory feedback and to provide updates, including adding an exploratory objective and endpoint, to add study visits, to clarify options for participants at the end of the study and if their blind is broken, and to clarify statistical analysis for the key secondary endpoints. In addition, several editorial changes were made to clarify and correct the text.
24 March 2020	The overall reason for this amendment was the closure of the study. The protocol was amended to allow continuation of treatment for those participants already on study and to allow further enrollment up to approximately 30 participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated early due to low enrollment and missing efficacy assessment data due to missed visits related to COVID-19.

Notes: