Clinical trial results:
A Phase 3, randomized, double-blind, placebo-controlled, crossover study to assess the efficacy and safety of UX007 in the treatment of movement disorders associated with Glucose Transporter Type 1 Deficiency Syndrome (Glut1 DS)

Summary

EudraCT number	2015-005536-17
Trial protocol	DE ES FR GB IT
Global end of trial date	09 October 2019

Results information

Result version number	v1 (current)
This version publication date	24 April 2020
First version publication date	24 April 2020

Trial information

Trial identification

Sponsor protocol code	UX007G-CL301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02960217
WHO universal trial number (UTN)	-
Other trial identifiers	EMA/190573: Unique Product Identifier (UPI)

Notes:

Sponsors

Sponsor organisation name	Ultragenyx Pharmaceutical Inc.
Sponsor organisation address	60 Leveroni Court, Novato, United States, California 94949
Public contact	Medical Information, Ultragenyx Pharmaceutical Inc, +1 888-756-8657, medinfo@ultragenyx.com
Scientific contact	Medical Information, Ultragenyx Pharmaceutical Inc, +1 888-756-8657, medinfo@ultragenyx.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	09 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 October 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary Objectives:
•Evaluate the efficacy and safety of UX007 in the treatment of disabling paroxysmal movement disorders associated with Glut1 DS

Protection of trial subjects:

The trial was designed, conducted, recorded, and reported in accordance with the principles established by the 18th World Medical Association General Assembly (Helsinki, 1964) and subsequent amendments and clarifications adopted by the General Assemblies. The investigators made every effort to ensure that the study was conducted in full conformance with Helsinki principles, international Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines, current Food and Drug Administration (FDA) regulations, EU Clinical Trial Directive 2001/20/EC, and local ethical and regulatory requirements. Each investigator was thoroughly familiar with the appropriate administration and potential risks of administration of the study drug, as described in the protocol and Investigator's Brochure, prior to the initiation of the study. The method of obtaining and documenting informed consent and the contents of the informed consent form (ICF) complied with ICH GCP guidelines, the requirements of 21 CFR Part 50, "Protection of Human Subjects," the Health Insurance Portability and Accountability Act regulations, and all other applicable regulatory requirements. Investigators were responsible for preparing the ICF and submitting it to the Sponsor for approval prior to submission to the Institutional Review Board (IRB). All ICFs were written in regional language and contained the minimum elements for consent as mandated by the ICH guidelines. An IRB-approved ICF was provided by the Sponsor prior to initiation of the study. Investigators obtained signed written informed consent from each potential study subject prior to the conduct of any study procedures and after the methods, objectives, requirements, and potential risks of the study were fully explained to each potential subject. Consent for participation could be withdrawn at any time for any reason by the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 April 2017
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	France: 8
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 15
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	44
EEA total number of subjects	29

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)	7
Adolescents (12-17 years)	9
Adults (18-64 years)	28
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During a 6-week Run-in Period, subjects recorded disabling paroxysmal movement disorder events in a daily electronic Glut1 DS movement disorder diary.

Pre-assignment period milestones

Number of subjects started	44
Number of subjects completed	43

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Randomized not treated: 1

Period 1

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

Blinding implementation details:

Double-blind conditions were established during this period so that neither the sponsor, subject, or site personnel involved in study conduct knew the identity of a subject's treatment. After all subjects completed the double-blind period, unblinding of the study occurred.

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-Blind UX007 Followed by Placebo

Arm description:

Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks. After a washout period of 2 weeks, they then received placebo for 10 weeks.

Arm type	Experimental
Investigational medicinal product name	triheptanoin
Investigational medicinal product code	UX007
Other name	C7 oil, glycerol triheptanoate, glycerol trienanthate, 1, 2, 3-trienanthoylglycerol, trienanthin, 2,3-di(heptanoyloxy)propyl heptanoate
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

The total daily dose was divided into 4 equal doses mixed with food or drink (or formula, as appropriate), and administered orally or by gastronomy tube at breakfast, lunch, dinner, and before bed.

Arm title	Double-Blind Placebo Followed by UX007

Arm description:

Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks. After a washout period of 2 weeks, they then received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Arm type	Experimental

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	safflower oil
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

The total daily dose was divided into 4 equal doses mixed with food or drink (or formula, as appropriate), and administered orally or by gastronomy tube at breakfast, lunch, dinner, and before bed.

Number of subjects in period 1[1]	Double-Blind UX007 Followed by Placebo	Double-Blind Placebo Followed by UX007
Started	22	21
Completed	21	21
Not completed	1	0
Adverse event	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One subject was randomized but did not receive any treatment due to a protocol violation; this subject was not included in any analyses in this study.

Period 2

Period 2 title	Maintenance Phase: Crossover Washout
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-Blind UX007 Followed by Placebo

Arm description:

Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks. After a washout period of 2 weeks, they then received placebo for 10 weeks.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Double-Blind Placebo Followed by UX007

Arm description:

Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks. After a washout period of 2 weeks, they then received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Double-Blind UX007 Followed by Placebo	Double-Blind Placebo Followed by UX007
Started	21	21
Completed	21	21

Period 3

Period 3 title	Maintenance Phase: Treatment Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Double-blind conditions were established during this period so that neither the sponsor, subject, or site personnel involved in study conduct knew the identity of a subject's treatment. After all subjects completed the double-blind period, unblinding of the study occurred.

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-Blind UX007 Followed by Placebo

Arm description:

Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks. After a washout period of 2 weeks, they then received placebo for 10 weeks.

Arm type	Experimental
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	safflower oil
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

The total daily dose was divided into 4 equal doses mixed with food or drink (or formula, as appropriate), and administered orally or by gastronomy tube at breakfast, lunch, dinner, and before bed.

Arm title	Double-Blind Placebo Followed by UX007

Arm description:

Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks. After a washout period of 2 weeks, they then received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Arm type	Experimental
Investigational medicinal product name	triheptanoin
Investigational medicinal product code	UX007
Other name	C7 oil, glycerol triheptanoate, glycerol trienanthate, 1, 2, 3-trienanthoylglycerol, trienanthin, 2,3-di(heptanoyloxy)propyl heptanoate
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

The total daily dose was divided into 4 equal doses mixed with food or drink (or formula, as appropriate), and administered orally or by gastronomy tube at breakfast, lunch, dinner, and before bed.

Number of subjects in period 3	Double-Blind UX007 Followed by Placebo	Double-Blind Placebo Followed by UX007
Started	21	21
Completed	20	18
Not completed	1	3
Consent withdrawn by subject	-	1
Other, not specified	-	1
Adverse event	-	1
Lack of efficacy	1	-

Period 4

Period 4 title	Open-Label Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Double-Blind UX007 Followed by Placebo-->Open Label UX007

Arm description:

Subjects had the option of rolling into the Open-Label Extension Phase, to continue UX007 treatment for up to 3 years.

Arm type	Experimental
Investigational medicinal product name	triheptanoin
Investigational medicinal product code	UX007
Other name	C7 oil, glycerol triheptanoate, glycerol trienanthate, 1, 2, 3-trienanthoylglycerol, trienanthin, 2,3-di(heptanoyloxy)propyl heptanoate
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

The total daily dose was divided into 4 equal doses mixed with food or drink (or formula, as appropriate), and administered orally or by gastronomy tube at breakfast, lunch, dinner, and before bed.

Arm title	Double-Blind Placebo Followed by UX007-->Open Label UX007

Arm description:

Subjects had the option of rolling into the Open-Label Extension Phase, to continue UX007 treatment for up to 3 years.

Arm type	Experimental
Investigational medicinal product name	triheptanoin
Investigational medicinal product code	UX007
Other name	C7 oil, glycerol triheptanoate, glycerol trienanthate, 1, 2, 3-trienanthoylglycerol, trienanthin, 2,3-di(heptanoyloxy)propyl heptanoate
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

The total daily dose was divided into 4 equal doses mixed with food or drink (or formula, as appropriate), and administered orally or by gastronomy tube at breakfast, lunch, dinner, and before bed.

Number of subjects in period 4[2]	Double-Blind UX007 Followed by Placebo-->Open Label UX007	Double-Blind Placebo Followed by UX007-->Open Label UX007
Started	20	13
Completed	0	0
Not completed	20	13
Other, not specified	-	1
Adverse event	1	-
Sponsor decision	18	11
Lack of efficacy	1	1

Notes:

[2] - 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: 5 subjects completed the double blind period but did not continue in the open label period.

Baseline characteristics

Reporting groups	
Reporting group title	Double-Blind UX007 Followed by Placebo
Reporting group description:	
Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks. After a washout period of 2 weeks, they then received placebo for 10 weeks.	
Reporting group title	Double-Blind Placebo Followed by UX007
Reporting group description:	
Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks. After a washout period of 2 weeks, they then received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.	

Reporting group values	Double-Blind UX007 Followed by Placebo	Double-Blind Placebo Followed by UX007	Total
Number of subjects	22	21	43
Age categorical Units: Subjects			
< 18 years old	7	9	16
>= 18 years old	15	12	27
Age continuous Units: years			
arithmetic mean	23.41	18.37	
standard deviation	± 13.156	± 5.730	-
Gender categorical Units: Subjects			
Female	12	12	24
Male	10	9	19
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	17	17	34
Unknown or Not Reported	4	4	8
Race Units: Subjects			
Black or African American	0	1	1
White	18	16	34
Missing	4	4	8

End points

End points reporting groups

Reporting group title	Double-Blind UX007 Followed by Placebo

Reporting group description:

Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks. After a washout period of 2 weeks, they then received placebo for 10 weeks.

Reporting group title	Double-Blind Placebo Followed by UX007

Reporting group description:

Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks. After a washout period of 2 weeks, they then received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Reporting group title	Double-Blind UX007 Followed by Placebo

Reporting group description:

Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks. After a washout period of 2 weeks, they then received placebo for 10 weeks.

Reporting group title	Double-Blind Placebo Followed by UX007

Reporting group description:

Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks. After a washout period of 2 weeks, they then received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Reporting group title	Double-Blind UX007 Followed by Placebo

Reporting group description:

Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks. After a washout period of 2 weeks, they then received placebo for 10 weeks.

Reporting group title	Double-Blind Placebo Followed by UX007

Reporting group description:

Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks. After a washout period of 2 weeks, they then received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Reporting group title	Double-Blind UX007 Followed by Placebo-->Open Label UX007

Reporting group description:

Subjects had the option of rolling into the Open-Label Extension Phase, to continue UX007 treatment for up to 3 years.

Reporting group title	Double-Blind Placebo Followed by UX007-->Open Label UX007

Reporting group description:

Subjects had the option of rolling into the Open-Label Extension Phase, to continue UX007 treatment for up to 3 years.

Subject analysis set title	Full Analysis Set: Double-Blind UX007
Subject analysis set type	Full analysis

Subject analysis set description:

UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Full Analysis Set: all randomized subjects who received at least 1 dose of study drug.

Subject analysis set title	Full Analysis Set: Double-Blind Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo for 10 weeks.

Full Analysis Set: all randomized subjects who received at least 1 dose of study drug.

Subject analysis set title	Safety Analysis Set: Double-Blind UX007
Subject analysis set type	Safety analysis

Subject analysis set description:

UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Safety Analysis Set: all randomized subjects who received at least 1 dose of study drug.

Subject analysis set title	Safety Analysis Set: Double-Blind Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

Placebo for 10 weeks.

Safety Analysis Set: all randomized subjects who received at least 1 dose of study drug.

Subject analysis set title	Safety Analysis Set: Open-Label UX007
Subject analysis set type	Safety analysis

Subject analysis set description:

UX007 treatment continuation for up to 3 years.

Safety Analysis Set: all randomized participants who received at least 1 dose of study drug.

Primary: Maintenance Phase Movement Disorder Frequency

End point title	Maintenance Phase Movement Disorder Frequency[1]

End point description:

The frequency of paroxysmal movement disorders captured as disabling movement disorder events (normalized to a 4-week rate) observed during the Maintenance Phase in participants treated with UX007 versus placebo, as recorded by the subject/caregiver in an event-based daily Glut1 DS symptom diary.

End point type	Primary

End point timeframe:

Maintenance Phase (up to Week 22)

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: Statistical analyses are attached as a pdf.

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	42		
Units: movement disorder events per 4 weeks				
median (full range (min-max))	14.26 (0.0 to 112.0)	11.81 (0.5 to 112.0)		

Attachments (see zip file)	Statistical Analysis for Maintenance Phase Movement Disorder

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, and Discontinuations Due to TEAEs

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, and Discontinuations Due to TEAEs[2]

End point description:

An Adverse Event (AE) was defined as any untoward medical occurrence, whether or not considered drug related. Serious adverse events (SAE) was defined as an AE that at any dose, in the view of either the Investigator or Ultragenyx, results in any of the following outcomes: death; a life-threatening AE; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant incapacity or disability (substantial disruption of the ability to conduct normal life functions); a congenital anomaly/birth defect; other important medical event. All reported AEs with with a start date that occurred or worsened in severity on or after the first dose of study drug in the corresponding treatment period and before the first dose of study drug in the next treatment period were defined as TEAEs. AEs were graded as 1=mild, 2=moderate, 3=severe, 4=life=threatening, 5=death.

End point type	Primary

End point timeframe:

From first dose of study drug through 30-35 days after final dose. Mean (SD) treatment duration was 65.7 (12.06) and 68.3 (7.04) days for double-blind UX007 and placebo, and 305.0 (122.71) days for open-label UX007.

Notes:

[2] - 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: Descriptive statistics are presented per protocol.

End point values	Safety Analysis Set: Double-Blind UX007	Safety Analysis Set: Double-Blind Placebo	Safety Analysis Set: Open-Label UX007	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	43	42	33	
Units: subjects				
TEAEs	40	34	28	
Serious TEAEs	2	1	2	
Treatment-Related TEAEs	33	19	17	
Treatment-Related Serious TEAEs	1	0	0	
Grade 3 or 4 TEAEs	4	3	3	
Grade 4 TEAEs	0	0	0	
Gastrointestinal TEAEs	32	17	18	
TEAEs Leading to Treatment Discontinuation	2	1	0	
TEAEs Leading to Study Discontinuation	2	1	0	
TEAEs Leading to Death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Baseline and Post-Baseline Columbia Suicide Severity Rating Scale (C-SSRS) Responses During Double-Blind Treatment Period

End point title	Baseline and Post-Baseline Columbia Suicide Severity Rating Scale (C-SSRS) Responses During Double-Blind Treatment Period[3]

End point description:

The C-SSRS is a participant-rated questionnaire to assess suicidal ideation, suicidal behavior, and self-injurious behavior with no suicidal intent (yes or no responses). Positive responses (i.e., 'Yes') to C-SSRS questions correspond to events in these categories with the exception of the category 'No events'. Suicidal ideation includes the following subcategories: passive; active-nonspecific; active-method/no intent/no plan; active-intent/with or without method/no plan; active-method/intent/plan. Suicidal behavior includes the following subcategories: suicide attempt; interrupted attempt; aborted attempt; preparatory actions toward immanent suicidal behaviors; completed suicide. Suicidal ideation and/or suicidal behavior category includes participants with positive responses in the category suicidal ideation

and/or suicidal behavior.

End point type	Primary

End point timeframe:

Baseline, up to Week 22

Notes:

[3] - 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: Descriptive statistics are presented per protocol.

End point values	Safety Analysis Set: Double-Blind UX007	Safety Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40[4]	40[5]		
Units: participants				
BL: No Events	38	38		
PB: No Events	40	39		
BL: Suicidal Ideation	1	1		
PB: Suicidal Ideation	0	0		
BL: Suicidal Behavior	1	1		
PB: Suicidal Behavior	0	1		
BL: Suicidal Ideation and/or Behavior	2	2		
PB: Suicidal Ideation and/or Behavior	0	1		
BL: Self-Injurious Behavior, No Suicidal Intent	1	1		
PB: Self-Injurious Behavior, No Suicidal Intent	0	1		

Notes:

[4] - Subjects with a baseline (BL) and postbaseline (PB) assessment

[5] - Subjects with a baseline (BL) and postbaseline (PB) assessment

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in 12 Minute Walk Test (12MWT) Distance at Treatment Week 10

End point title	Change From Period Baseline in 12 Minute Walk Test (12MWT) Distance at Treatment Week 10

End point description:

Walking capacity and endurance, as determined by the distance in meters walked in 12 minutes during the 12MWT.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	36[6]	38[7]		
Units: meters				
least squares mean (standard error)	-15.9 (± 25.63)	-33.0 (± 24.91)		

Notes:

[6] - subjects with an assessment

[7] - subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in 12MWT

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in Patient Reported Outcomes Measurement Information System (PROMIS) Health Assessment Questionnaire (Adult Form) Physical Function Score at Treatment Week 10

End point title	Change From Period Baseline in Patient Reported Outcomes Measurement Information System (PROMIS) Health Assessment Questionnaire (Adult Form) Physical Function Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015). It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Physical Function Mobility Domain, increases in score indicate greater mobility.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[8]	25[9]		
Units: T-score				
least squares mean (standard error)	-0.9 (± 0.67)	-0.9 (± 0.65)		

Notes:

[8] - adult subjects with an assessment

[9] - adult subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Fatigue Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Fatigue Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015). It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Fatigue Domain, decreases in score indicate less fatigue.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[10]	25[11]		
Units: T-score				
least squares mean (standard error)	2.9 (± 1.40)	0.9 (± 1.36)		

Notes:

[10] - adult subjects with an assessment

[11] - adult subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Sleep Disturbance Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Sleep Disturbance Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015). It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Sleep Disturbance Domain, decreases in score indicate less sleep disturbance.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[12]	25[13]		
Units: T-score				
least squares mean (standard error)	0.4 (± 1.24)	0.7 (± 1.20)		

Notes:

[12] - adult subjects with an assessment

[13] - adult subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Pain Interference Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Pain Interference Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015). It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Pain Interference Domain, decreases in scores indicate less pain interference.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[14]	25[15]		
Units: T-score				
least squares mean (standard error)	4.5 (± 1.64)	3.7 (± 1.58)		

Notes:

[14] - adult subjects with an assessment

[15] - adult subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Cognitive Function Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment

	Questionnaire (Adult Form) Cognitive Function Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015). It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. The Cognitive Function Domain measures cognitive function impairment. Decreases in score indicate less cognitive function impairment.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[16]	25[17]		
Units: T-score				
least squares mean (standard error)	2.0 (± 1.29)	1.2 (± 1.25)		

Notes:

[16] - adult subjects with an assessment

[17] - adult subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Social Roles and Activities Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Social Roles and Activities Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015). It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Social Roles and Activities Domain, decreases in score indicate worse /less or decrease of performance in social roles and activities.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[18]	25[19]		
Units: T-score				
least squares mean (standard error)	-4.1 (± 1.35)	-2.3 (± 1.32)		

Notes:

[18] - adult subjects with an assessment

[19] - adult subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Anxiety Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Adult Form) Anxiety Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015). It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Anxiety Domain, decreases in scores indicate less anxiety.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23[20]	25[21]		
Units: T-score				
least squares mean (standard error)	3.1 (± 1.49)	0.5 (± 1.45)		

Notes:

[20] - adult subjects with an assessment

[21] - adult subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Mobility Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment

	Questionnaire (Pediatric/Parent-Proxy Form) Mobility Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015) via parent/proxy. It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Mobility Domain, decreases in score indicate less mobility.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16[22]	13[23]		
Units: T-score				
least squares mean (standard error)	-1.0 (± 1.62)	0.0 (± 1.73)		

Notes:

[22] - pediatric subjects with an assessment

[23] - pediatric subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Upper Extremity Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Upper Extremity Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015) via parent/proxy. It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Upper Extremity Domain, decreases in score indicate less upper extremity movement.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16[24]	13[25]		
Units: T-score				
least squares mean (standard deviation)	-0.4 (± 1.91)	1.3 (± 2.11)		

Notes:

[24] - pediatric subjects with an assessment

[25] - pediatric subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Fatigue Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Fatigue Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015) via parent/proxy. It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Fatigue Domain, decreases in score indicate less fatigue.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16[26]	13[27]		
Units: T-score				
least squares mean (standard error)	-1.8 (± 2.40)	-0.6 (± 2.64)		

Notes:

[26] - pediatric subjects with an assessment

[27] - pediatric subjects with an assessment

Attachments (see zip file)	Statistical Analysis 2 for Change From Period Baseline in

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Pain Interference Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Pain Interference Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015) via parent/proxy. It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Pain Interference Domain, decreases in score indicate less pain interference.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16[28]	13[29]		
Units: T-score				
least squares mean (standard error)	3.2 (± 1.84)	1.6 (± 1.96)		

Notes:

[28] - pediatric subjects with an assessment

[29] - pediatric subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Peer Relationships Score at Treatment Week 10

End point title	Change From Period Baseline in PROMIS Health Assessment Questionnaire (Pediatric/Parent-Proxy Form) Peer Relationships Score at Treatment Week 10

End point description:

The PROMIS was developed by the National Institutes of Health and uses domain-specific measures to assess patient well-being (Broderick et al. 2013; NIH 2015) via parent/proxy. It uses a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population. For the Peer Relationships Domain, decreases in score indicate worse functioning in peer relationships.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16[30]	13[31]		
Units: T-score				
least squares mean (standard error)	2.0 (± 1.57)	-0.0 (± 1.64)		

Notes:

[30] - pediatric subjects with an assessment

[31] - pediatric subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in PROMIS

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression - Improvement (CGI-I) at Treatment Week 10

End point title	Clinical Global Impression - Improvement (CGI-I) at Treatment Week 10

End point description:

Participant/caregiver global impression of change in clinical status using the CGI-I. The CGI-I is a 7-point scale that assesses how much the participant's condition has improved or worsened relative to a baseline state at the beginning of the intervention and rated as: 1=very much better; 2=much better; 3=a little better; 4=no change; 5=a little worse; 6=much worse; 7=very much worse.

End point type	Secondary

End point timeframe:

Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	40		
Units: score on a scale				
least squares mean (standard error)	3.5 (± 0.20)	3.6 (± 0.20)		

Attachments (see zip file)	Statistical Analysis for Clinical Global Impression -

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Movement Disorder Events During Maintenance Phase

End point title	Duration of Movement Disorder Events During Maintenance Phase

End point description:

Duration of disabling paroxysmal movement disorder events observed during the Maintenance Period of treatment, as recorded by the subject/caregiver in an event-based daily electronic Glut1 DS symptom

diary.

End point type	Secondary

End point timeframe:

Maintenance Phase (up to 22 weeks)

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	43	42		
Units: hours				
arithmetic mean (standard deviation)	0.9 (± 1.98)	0.7 (± 1.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in Cambridge Neuropsychological Test Automated Battery (CANTAB), Spatial Span (SSP) Span Length Scores at Treatment Week 10

End point title	Change From Period Baseline in Cambridge Neuropsychological Test Automated Battery (CANTAB), Spatial Span (SSP) Span Length Scores at Treatment Week 10

End point description:

Cognitive function as measured by the CANTAB. CANTAB measures neuropsychological function using a standardized, computerized battery of tests designed to assess visual memory, working memory, new learning and reaction time. SSP Span Length assesses the cognitive domain of sequential memory, with scores on a discrete, ordinal scale from 2 to 9; higher scores indicate better function.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	14		
Units: units on a scale				
least squares mean (standard error)	0.1 (± 0.31)	0.6 (± 0.29)		

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in CANTAB, Spatial Working Memory Between Errors (SWMBE) Scores at Treatment Week 10

End point title	Change From Period Baseline in CANTAB, Spatial Working Memory Between Errors (SWMBE) Scores at Treatment Week 10

End point description:

CANTAB measures neuropsychological function using a standardized, computerized battery of tests designed to assess visual memory, working memory, new learning and reaction time. SWMBE assesses the cognitive domain of working memory, with scores on a discrete, ordinal scale from 0 to 360; lower scores indicate better function.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	14		
Units: units on a scale				
least squares mean (standard error)	-0.2 (± 2.94)	0.2 (± 2.83)		

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Period Baseline in CANTAB, Spatial Working Memory Strategy (SWMS) Scores at Treatment Week 10

End point title	Change From Period Baseline in CANTAB, Spatial Working Memory Strategy (SWMS) Scores at Treatment Week 10

End point description:

CANTAB measures neuropsychological function using a standardized, computerized battery of tests designed to assess visual memory, working memory, new learning and reaction time. SWMS assesses the cognitive domain of executive function/strategy, with scores on a discrete, ordinal scale from 4 to 28; lower scores indicate better function.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13[32]	14[33]		
Units: units on a scale				
least squares mean (standard error)	0.6 (± 0.77)	-0.4 (± 0.74)		

Notes:

[32] - subjects with an assessment

[33] - subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Period Baseline in

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CANTAB, Paired Associates Learning Total Errors (PALTEA) at Treatment Week 10

End point title	Change From Baseline in CANTAB, Paired Associates Learning Total Errors (PALTEA) at Treatment Week 10

End point description:

CANTAB measures neuropsychological function using a standardized, computerized battery of tests designed to assess visual memory, working memory, new learning and reaction time. PALTEA assesses the cognitive domain of episodic memory/new learning, with scores on a discrete, ordinal scale from 0 to 137; lower scores indicate better function.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13[34]	15[35]		
Units: units on a scale				
least squares mean (standard error)	-2.0 (± 4.74)	-8.5 (± 4.41)		

Notes:

[34] - subjects with an assessment

[35] - subjects with an assessment

Attachments (see zip file)	Statistical Analysis 2 for Change From Baseline in CANTAB,

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CANTAB, Paired Associates Learning First Trial Memory Score (PALFTMS) at Treatment Week 10

End point title	Change From Baseline in CANTAB, Paired Associates Learning First Trial Memory Score (PALFTMS) at Treatment Week 10

End point description:

CANTAB measures neuropsychological function using a standardized, computerized battery of tests designed to assess visual memory, working memory, new learning and reaction time. PALFTMS assesses the cognitive domain of episodic memory, with scores on a discrete, ordinal scale from 0 to 27; higher scores indicate better function.

End point type	Secondary

End point timeframe:

Period Baseline (defined as the last non-missing assessment prior to or on the date of the first dose of study drug for each double-blind Treatment Period), Week 10

End point values	Full Analysis Set: Double-Blind UX007	Full Analysis Set: Double-Blind Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13[36]	15[37]		
Units: units on a scale				
least squares mean (standard error)	-0.1 (± 1.12)	0.9 (± 1.04)		

Notes:

[36] - subjects with an assessment

[37] - subjects with an assessment

Attachments (see zip file)	Statistical Analysis for Change From Baseline in CANTAB,

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through 30-35 days after final dose. Mean (SD) treatment duration was 65.7 (12.06) and 68.3 (7.04) days for double-blind UX007 and placebo, respectively, and 305.0 (122.71) days for open-label UX007.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	DB UX007

Reporting group description:

Double-Blind Maintenance Phase: Subjects received UX007 (dosed according to an age- and weight-based strategy, up to a maximum daily administration of 130 g) for 10 weeks.

Reporting group title	OL UX007

Reporting group description:

Open-Label Extension Phase: Subjects continued UX007 treatment for up to 3 years.

Reporting group title	DB Placebo

Reporting group description:

Double-Blind Maintenance Phase: Subjects received placebo for 10 weeks.

Serious adverse events	DB UX007	OL UX007	DB Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 43 (4.65%)	2 / 33 (6.06%)	1 / 42 (2.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Head Injury			
subjects affected / exposed	1 / 43 (2.33%)	0 / 33 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Movement Disorder			
subjects affected / exposed	1 / 43 (2.33%)	1 / 33 (3.03%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor Hyperactivity			

subjects affected / exposed	0 / 43 (0.00%)	0 / 33 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Limb Asymmetry			
subjects affected / exposed	0 / 43 (0.00%)	1 / 33 (3.03%)	0 / 42 (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

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

Non-serious adverse events	DB UX007	OL UX007	DB Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 43 (83.72%)	22 / 33 (66.67%)	26 / 42 (61.90%)
Investigations			
Blood Ketone Body Increased			
subjects affected / exposed	3 / 43 (6.98%)	0 / 33 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
Weight Increased			
subjects affected / exposed	3 / 43 (6.98%)	2 / 33 (6.06%)	1 / 42 (2.38%)
occurrences (all)	3	2	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 43 (2.33%)	2 / 33 (6.06%)	2 / 42 (4.76%)
occurrences (all)	1	2	2
Dyskinesia			
subjects affected / exposed	3 / 43 (6.98%)	3 / 33 (9.09%)	2 / 42 (4.76%)
occurrences (all)	3	4	2
Headache			
subjects affected / exposed	7 / 43 (16.28%)	6 / 33 (18.18%)	6 / 42 (14.29%)
occurrences (all)	15	17	12
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 43 (6.98%)	3 / 33 (9.09%)	5 / 42 (11.90%)
occurrences (all)	3	5	5

Gait Disturbance			
subjects affected / exposed	0 / 43 (0.00%)	2 / 33 (6.06%)	1 / 42 (2.38%)
occurrences (all)	0	2	1
Pyrexia			
subjects affected / exposed	4 / 43 (9.30%)	2 / 33 (6.06%)	1 / 42 (2.38%)
occurrences (all)	5	2	1
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	4 / 43 (9.30%)	0 / 33 (0.00%)	0 / 42 (0.00%)
occurrences (all)	10	0	0
Abdominal Pain			
subjects affected / exposed	6 / 43 (13.95%)	5 / 33 (15.15%)	1 / 42 (2.38%)
occurrences (all)	9	6	1
Abdominal Pain Upper			
subjects affected / exposed	14 / 43 (32.56%)	7 / 33 (21.21%)	6 / 42 (14.29%)
occurrences (all)	35	22	11
Anal Incontinence			
subjects affected / exposed	3 / 43 (6.98%)	0 / 33 (0.00%)	0 / 42 (0.00%)
occurrences (all)	4	0	0
Constipation			
subjects affected / exposed	1 / 43 (2.33%)	3 / 33 (9.09%)	1 / 42 (2.38%)
occurrences (all)	1	5	1
Diarrhoea			
subjects affected / exposed	22 / 43 (51.16%)	9 / 33 (27.27%)	5 / 42 (11.90%)
occurrences (all)	50	46	12
Nausea			
subjects affected / exposed	7 / 43 (16.28%)	4 / 33 (12.12%)	5 / 42 (11.90%)
occurrences (all)	10	6	7
Vomiting			
subjects affected / exposed	13 / 43 (30.23%)	8 / 33 (24.24%)	8 / 42 (19.05%)
occurrences (all)	23	14	11
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 43 (4.65%)	3 / 33 (9.09%)	0 / 42 (0.00%)
occurrences (all)	2	4	0
Oropharyngeal Pain			

subjects affected / exposed	4 / 43 (9.30%)	1 / 33 (3.03%)	3 / 42 (7.14%)
occurrences (all)	4	1	3
Psychiatric disorders			
Aggression			
subjects affected / exposed	4 / 43 (9.30%)	0 / 33 (0.00%)	0 / 42 (0.00%)
occurrences (all)	4	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 43 (6.98%)	1 / 33 (3.03%)	0 / 42 (0.00%)
occurrences (all)	3	1	0
Gastroenteritis Viral			
subjects affected / exposed	0 / 43 (0.00%)	2 / 33 (6.06%)	1 / 42 (2.38%)
occurrences (all)	0	2	1
Influenza			
subjects affected / exposed	3 / 43 (6.98%)	2 / 33 (6.06%)	0 / 42 (0.00%)
occurrences (all)	3	3	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 43 (11.63%)	2 / 33 (6.06%)	2 / 42 (4.76%)
occurrences (all)	7	4	2
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	5 / 43 (11.63%)	1 / 33 (3.03%)	1 / 42 (2.38%)
occurrences (all)	5	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 September 2018	• Section 4.6 was included to define subgroups for analysis. Section 8.8.1 and Appendix A were updated with the statistical methods for analyses of the subgroups defined in Section 4.6. • Revised Section 5.8 to define PROMIS final T scores from the PROMIS online scoring system. • Revised SAP to align with changes to the Protocol made in Amendment 3.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported