



## Clinical trial results:

### A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Adaptive Study to Assess the Safety and Efficacy of UX007 in Subjects with Glucose Transporter Type 1 Deficiency Syndrome

#### Summary

EudraCT number	2013-003771-35
Trial protocol	IT GB FR HU ES DK
Global end of trial date	20 September 2017

#### Results information

Result version number	v1
This version publication date	27 February 2019
First version publication date	27 February 2019

#### Trial information

##### Trial identification

Sponsor protocol code	UX007G-CL201
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01993186
WHO universal trial number (UTN)	-

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	20 September 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 September 2017
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objectives of the study are to evaluate the efficacy of UX007 compared to placebo as measured by the reduction from randomization to week 8 in frequency of seizures and to evaluate the safety of UX007 via adverse event (AE) rates, laboratory values, and electrocardiogram (ECG).

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	28 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Israel: 3
Country: Number of subjects enrolled	United States: 18

Worldwide total number of subjects	36
EEA total number of subjects	11

Notes:

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### Subjects enrolled per age group

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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)	15
Adolescents (12-17 years)	13
Adults (18-64 years)	8
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Beginning with the Screening visit, subjects recorded seizure frequency during the 6-week Baseline Period. If the subject did not meet the seizure count criteria, the subject was considered a screen failure and was not randomized.

### Period 1

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

Blinding implementation details:

The investigator and site personnel remained blinded to the randomization code during the study. Treatment assignment for an individual subject would be unblinded by the Investigator only in an emergency, and only if knowledge of the treatment assignment were urgently needed for the clinical management or welfare of the subject.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	UX007

Arm description:

Subjects randomized to receive UX007 entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period.

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:

Treatment was mixed with food (or formula, if appropriate) and administered orally (PO) or by gastronomy tube at least four times per day (breakfast, lunch, dinner, and before bed).

<b>Arm title</b>	Placebo
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Arm description:

Subjects randomized to receive placebo entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period.

Arm type	Placebo
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:

Treatment was mixed with food (or formula, if appropriate) and administered PO or by gastronomy tube at least four times per day (breakfast, lunch, dinner, and before bed).

<b>Number of subjects in period 1</b>	UX007	Placebo
Started	25	11
Completed	23	11
Not completed	2	0
Consent withdrawn by subject	1	-
Protocol deviation	1	-

## Period 2

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

## Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	UX007

### Arm description:

Following completion of the Week 8 study visit, subjects continued treatment with open-label UX007 at the 35% dose level for an additional 44 weeks (Weeks 8-52).

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:

Treatment was mixed with food (or formula, if appropriate) and administered PO or by gastronomy tube at least four times per day (breakfast, lunch, dinner, and before bed).

<b>Arm title</b>	Placebo
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### Arm description:

Following completion of the Week 8 study visit, placebo subjects continued treatment with open-label UX007 at the 35% dose level for an additional 44 weeks (Weeks 8-52).

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:

Treatment was mixed with food (or formula, if appropriate) and administered PO or by gastronomy tube at least four times per day (breakfast, lunch, dinner, and before bed).

<b>Number of subjects in period 2</b>	UX007	Placebo
Started	23	11
Completed	16	5
Not completed	7	6
Consent withdrawn by subject	4	5
Subject non-compliance	1	-
Other, not specified	-	1
Adverse event	1	-
Principal investigator decision	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	UX007
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Reporting group description:

Subjects randomized to receive UX007 entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period.

Reporting group title	Placebo
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Reporting group description:

Subjects randomized to receive placebo entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period.

Reporting group values	UX007	Placebo	Total
Number of subjects	25	11	36
Age categorical			
Units: Subjects			
2 years to < 12 years	8	7	15
12 years to < 18 years	12	1	13
18 years to < 65 years	5	3	8
Age continuous			
Units: years			
arithmetic mean	13.86	15.24	
standard deviation	± 5.107	± 13.795	-
Gender categorical			
Units: Subjects			
Female	15	7	22
Male	10	4	14
Primary Race			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	1	0	1
Black or African American	0	1	1
Native Hawaiian or other Pacific Islander	0	0	0
White	23	9	32
Other (not specified)	1	0	1
Ethnicity			
Units: Subjects			
Hispanic or Latino	2	1	3
Not Hispanic or Latino	21	9	30
Unknown	2	1	3

## End points

### End points reporting groups

Reporting group title	UX007
Reporting group description: Subjects randomized to receive UX007 entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period.	
Reporting group title	Placebo
Reporting group description: Subjects randomized to receive placebo entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period.	
Reporting group title	UX007
Reporting group description: Following completion of the Week 8 study visit, subjects continued treatment with open-label UX007 at the 35% dose level for an additional 44 weeks (Weeks 8-52).	
Reporting group title	Placebo
Reporting group description: Following completion of the Week 8 study visit, placebo subjects continued treatment with open-label UX007 at the 35% dose level for an additional 44 weeks (Weeks 8-52).	
Subject analysis set title	Efficacy Analysis Set – 6MWT: UX007
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of subjects taking UX007 during the treatment period in the efficacy analysis set who had a baseline and at least 1 post baseline (Week 4 or Week 8) 6MWT assessment performed.	
Subject analysis set title	Efficacy Analysis Set - 6MWT: Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of subjects taking placebo during the treatment period in the efficacy analysis set who had a baseline and at least 1 post baseline (Week 4 or Week 8) 6MWT assessment performed.	
Subject analysis set title	Efficacy Analysis Set - GMFM-88: UX007
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of subjects taking UX007 during the treatment period in the efficacy analysis set who had a baseline and at least 1 post baseline (Week 4 or Week 8) GMFM-88 assessment performed.	
Subject analysis set title	Efficacy Analysis Set - GMFM-88: Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of subjects taking placebo during the treatment period in the efficacy analysis set who had a baseline and at least 1 post baseline (Week 4 or Week 8) GMFM-88 assessment performed.	
Subject analysis set title	Efficacy Analysis Set: UX007
Subject analysis set type	Full analysis
Subject analysis set description: All randomized subjects who received at least one dose of investigational product.	
Subject analysis set title	Efficacy Analysis Set: Placebo
Subject analysis set type	Full analysis
Subject analysis set description: All randomized subjects who received at least one dose of investigational product.	
Subject analysis set title	Safety Analysis Set: UX007
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects who received at least one dose of investigational product.	
Subject analysis set title	Safety Analysis Set: Placebo



Subject analysis set type	Safety analysis
Subject analysis set description: All subjects who received at least one dose of investigational product.	
Subject analysis set title	Efficacy Analysis Set - CANTAB: UX007
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of subjects taking UX007 during the treatment period in the efficacy analysis set who had a baseline and at least 1 post baseline (Week 4 or Week 8) CANTAB assessment performed.	
Subject analysis set title	Efficacy Analysis Set - CANTAB: Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subset of subjects taking placebo during the treatment period in the efficacy analysis set who had a baseline and at least 1 post baseline (Week 4 or Week 8) CANTAB assessment performed.	

### **Primary: Percent Reduction from Baseline to Week 8 in Frequency of Total Seizures (Normalized to a 4-Week Rate)**

End point title	Percent Reduction from Baseline to Week 8 in Frequency of Total Seizures (Normalized to a 4-Week Rate)
End point description: Reduction from baseline to Week 8 in frequency of seizures (normalized to a 4-week rate): observable seizures measured for 6 weeks after 2-week titration by diary and absence seizures measured overnight by electroencephalography (EEG). Seizure types include: generalized tonic-clonic, generalized tonic, generalized clonic, generalized atonic, partial/focal with secondary generalization, myoclonic, myoclonic atonic, myoclonic tonic, complex partial/focal, simple partial/focal motor and absence seizures.	
End point type	Primary
End point timeframe: Baseline, Week 8	

<b>End point values</b>	Efficacy Analysis Set: UX007	Efficacy Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: percent reduction of total seizures				
median (full range (min-max))	12.6 (-651 to 100)	0.0 (-1021 to 100)		

### **Statistical analyses**

<b>Statistical analysis title</b>	Between Group Comparison
Statistical analysis description: Hodges-Lehmann estimate of the location shift with 90% CI is based on Wilcoxon rank-sum test.	
Comparison groups	Efficacy Analysis Set: Placebo v Efficacy Analysis Set: UX007

Number of subjects included in analysis	36
Analysis specification	Post-hoc
Analysis type	superiority
Parameter estimate	Hodges-Lehmann estimate
Point estimate	13.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.63
upper limit	80.95

**Primary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs and Discontinuations Due to TEAEs During the Placebo-Controlled Period**

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs), Serious TEAEs and Discontinuations Due to TEAEs During the Placebo-Controlled Period <sup>[1]</sup>
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End point description:

An adverse event (AE) was defined as any untoward medical occurrence, whether or not considered drug related. An SAE was defined as an AE or suspected adverse reaction that at any dose resulted in any of the following outcomes: death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital anomaly/birth defect, or an important medical event that may have jeopardized the subject and may have required medical or surgical intervention to prevent one of the outcomes listed in the definition. An AE was considered a TEAE if it occurred or worsened in severity on or after the date of the first dose of study drug. An AE was considered a UX007 emergent adverse event if it occurred or worsened in severity on or after the first date of first dose of UX007 during the study.

End point type	Primary
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End point timeframe:

Weeks 0 to 8

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: Descriptive statistics are presented per protocol.

End point values	Safety Analysis Set: UX007	Safety Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: subjects				
TEAE	22	9		
Serious TEAE	1	0		
Grade 3 or 4 TEAE	2	0		
TEAE Leading to Study Discontinuation	0	0		
TEAE Leading to Death	0	0		
Gastrointestinal TEAE	18	5		
Related TEAE	18	5		
Related Serious TEAE	0	0		
Related Gastrointestinal TEAE	17	4		
UX007 Emergent AE	22	0		
Serious UX007 Emergent AE	1	0		

## Statistical analyses

No statistical analyses for this end point

### Primary: Number of Subjects With TEAEs, Serious TEAEs and Discontinuations Due to TEAEs During the Extension Period

End point title	Number of Subjects With TEAEs, Serious TEAEs and Discontinuations Due to TEAEs During the Extension Period <sup>[2]</sup>
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End point description:

An AE was defined as any untoward medical occurrence, whether or not considered drug related. An SAE was defined as an AE or suspected adverse reaction that at any dose resulted in any of the following outcomes: death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital anomaly/birth defect, or an important medical event that may have jeopardized the subject and may have required medical or surgical intervention to prevent one of the outcomes listed in the definition. An AE was considered a TEAE if it occurred or worsened in severity on or after the date of the first dose of study drug. An AE was considered a UX007 emergent adverse event if it occurred or worsened in severity on or after the first date of first dose of UX007 during the study.

End point type	Primary
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End point timeframe:

Weeks 9 to 52 plus 30 days

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: UX007	Safety Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	11		
Units: subjects				
TEAE	21	11		
Serious TEAE	2	0		
Grade 3 or 4 TEAE	1	0		
TEAE Leading to Study Discontinuation	1	0		
TEAE Leading to Death	0	0		
Gastrointestinal TEAE	15	10		
Related TEAE	19	8		
Related Serious TEAE	0	0		
Related Gastrointestinal TEAE	13	8		
UX007 Emergent AE	21	11		
Serious UX007 Emergent AE	2	0		

## Statistical analyses

**Secondary: Percent Reduction From Baseline to Week 8 in Frequency of Observable Seizures (Normalized to a 4-Week Rate)**

End point title	Percent Reduction From Baseline to Week 8 in Frequency of Observable Seizures (Normalized to a 4-Week Rate)
End point description:	
Observable generalized and partial-onset seizures measured for 6 weeks by diary. Seizure types include: generalized tonic-clonic, generalized tonic, generalized clonic, generalized atonic, partial/focal with secondary generalization, myoclonic, myoclonic atonic, myoclonic tonic, complex partial/focal, simple partial/focal motor, simple partial/focal sensory and simple partial/focal psychological.	
End point type	Secondary
End point timeframe:	
Baseline (approximately 6 weeks between the day of the screening visit and the day prior to the randomization visit), Week 8 (approximately 6 weeks between the day of the end of titration visit and the day prior to the week 8 visit)	

End point values	Efficacy Analysis Set: UX007	Efficacy Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17 <sup>[3]</sup>	10 <sup>[4]</sup>		
Units: percent reduction in seizures				
median (full range (min-max))	0.0 (-651 to 84)	0.0 (-1021 to 75)		

Notes:

[3] - observable seizures subjects

[4] - observable seizures subjects

**Statistical analyses**

Statistical analysis title	Between Group Comparison
Statistical analysis description:	
Hodges-Lehmann estimate of the location shift with 90% CI is based on Wilcoxon rank-sum test.	
Comparison groups	Efficacy Analysis Set: UX007 v Efficacy Analysis Set: Placebo
Number of subjects included in analysis	27
Analysis specification	Post-hoc
Analysis type	superiority
Parameter estimate	Hodges-Lehmann estimate
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-51.23
upper limit	84.25

**Secondary: Percent Reduction From Baseline to Week 8 in Frequency of Absence Seizures (Normalized to a 4-Week Rate)**

End point title	Percent Reduction From Baseline to Week 8 in Frequency of
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## End point description:

Absence seizures measured overnight by EEG. Seizure types include: absence awake ( $\geq 10$  sec), absence sleep ( $\geq 10$  sec), indeterminate absence awake (3-10 sec), and indeterminate absence sleep (3-10 sec)

## End point type

Secondary

## End point timeframe:

Baseline, Week 8

End point values	Efficacy Analysis Set: UX007	Efficacy Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17 <sup>[5]</sup>	6 <sup>[6]</sup>		
Units: percent reduction in seizures				
median (full range (min-max))	0.0 (-2400 to 100)	0.0 (0 to 100)		

## Notes:

[5] - absence seizure subjects

[6] - absence seizure subjects

## Statistical analyses

## Statistical analysis title

Between Group Comparison

## Statistical analysis description:

Hodges-Lehmann estimate of the location shift with 90% CI is based on Wilcoxon rank-sum test.

Comparison groups	Efficacy Analysis Set: UX007 v Efficacy Analysis Set: Placebo
Number of subjects included in analysis	23
Analysis specification	Post-hoc
Analysis type	superiority
Parameter estimate	Hodges-Lehmann estimate
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	37.5

### Secondary: Percentage of Subjects With at Least a 50% Reduction From Baseline to Week 8 in Frequency of Seizures

## End point title

Percentage of Subjects With at Least a 50% Reduction From Baseline to Week 8 in Frequency of Seizures

## End point description:

Seizure response rate, defined as the percentage of subjects with at least 50% reduction from randomization to week 8 in frequency of seizures. Observable generalized and partial-onset seizures measured for 6 weeks by diary and absence seizures measured overnight by EEG.

## End point type

Secondary

## End point timeframe:

Baseline, Week 8

End point values	Efficacy Analysis Set: UX007	Efficacy Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: percentage of subjects				
number (not applicable)	20.0	36.4		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With at Least 50% Reduction From Baseline to Week 8 in Frequency of Observable Seizures

End point title	Percentage of Subjects With at Least 50% Reduction From Baseline to Week 8 in Frequency of Observable Seizures
End point description: Observable seizure response, at least 50% reduction from baseline in frequency of observable seizures measured by diary, is defined as percent reduction in observable seizure frequency greater than or equal to 50%.	
End point type	Secondary
End point timeframe: Baseline, Week 8	

End point values	Efficacy Analysis Set: UX007	Efficacy Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: percentage of subjects				
number (not applicable)	4.0	27.3		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With at Least 50% Reduction From Baseline to Week 8 in Frequency of Absence Seizures

End point title	Percentage of Subjects With at Least 50% Reduction From Baseline to Week 8 in Frequency of Absence Seizures
End point description: Absence seizure response, at least 50% reduction from baseline in frequency of absence seizures measured overnight by EEG, is defined as percent reduction in absence seizure frequency greater than	

or equal to 50%.

End point type	Secondary
End point timeframe:	
Baseline, Week 8	

End point values	Efficacy Analysis Set: UX007	Efficacy Analysis Set: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	9		
Units: percentage of subjects				
number (not applicable)	20.0	11.1		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline to Week 8 in Cambridge Neuropsychological Test Automated Battery (CANTAB), Reaction Time (RTI) Scores, Generalized Estimating Equation (GEE)

End point title	Change From Baseline to Week 8 in Cambridge Neuropsychological Test Automated Battery (CANTAB), Reaction Time (RTI) Scores, Generalized Estimating Equation (GEE)
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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. RTI Simple choice reaction time standard deviation (RTISRTSD) assesses the cognitive domain of attention, with scores on a continuous range from 0 to 5000; lower scores indicate better function. RTI median simple choice reaction time (RTIMDSRT) assesses the cognitive domain of reaction time, with scores on a continuous range from 100 to 5100; lower scores indicate better function. RTI median 5-choice reaction time (RTIMDFRT) assesses the cognitive domain of reaction time, with scores on a continuous range from 100 to 5100; lower scores indicate better function. GEE statistical model.

End point type	Secondary
End point timeframe:	
Baseline, Week 8	

End point values	Efficacy Analysis Set - CANTAB: UX007	Efficacy Analysis Set - CANTAB: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: units on a scale				
least squares mean (standard error)				
RTISRTSD	41.698 (± 42.3539)	44.082 (± 53.3552)		
RTIMDSRT	15.512 (± 15.9204)	-48.157 (± 48.8781)		

RTIMDFRT	-14.723 ( $\pm$ 14.1862)	49.112 ( $\pm$ 58.4722)		
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## Statistical analyses

<b>Statistical analysis title</b>	RTISRTSD
Comparison groups	Efficacy Analysis Set - CANTAB: UX007 v Efficacy Analysis Set - CANTAB: Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.486 <sup>[7]</sup>
Method	GEE model
Parameter estimate	Least squares mean difference
Point estimate	-2.384
Confidence interval	
level	90 %
sides	2-sided
lower limit	-114.44
upper limit	109.67
Variability estimate	Standard error of the mean
Dispersion value	68.1231

Notes:

[7] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

<b>Statistical analysis title</b>	RTIMDSRT
Comparison groups	Efficacy Analysis Set - CANTAB: UX007 v Efficacy Analysis Set - CANTAB: Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8849 <sup>[8]</sup>
Method	GEE model
Parameter estimate	Least squares mean difference
Point estimate	63.669
Confidence interval	
level	90 %
sides	2-sided
lower limit	-23.6
upper limit	150.94
Variability estimate	Standard error of the mean
Dispersion value	53.0537

Notes:

[8] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

<b>Statistical analysis title</b>	RTIMDFRT
Comparison groups	Efficacy Analysis Set - CANTAB: UX007 v Efficacy Analysis Set - CANTAB: Placebo



Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1463 <sup>[9]</sup>
Method	GEE model
Parameter estimate	Least squares mean difference
Point estimate	-63.835
Confidence interval	
level	90 %
sides	2-sided
lower limit	-163.59
upper limit	35.93
Variability estimate	Standard error of the mean
Dispersion value	60.6496

Notes:

[9] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

### Secondary: Change From Baseline to Week 8 in CANTAB, Paired Associates Learning (PAL) Scores, GEE

End point title	Change From Baseline to Week 8 in CANTAB, Paired Associates Learning (PAL) Scores, GEE
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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. PAL total errors adjusted (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. PAL first trial memory score (PALFTMS) assesses the cognitive domain of episodic memory, with scores on a discrete, ordinal scale from 0 to 27; higher scores indicate better function. GEE statistical model.

End point type	Secondary
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End point timeframe:

Baseline, Week 8

End point values	Efficacy Analysis Set - CANTAB: UX007	Efficacy Analysis Set - CANTAB: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: units on a scale				
least squares mean (standard error)				
PALTEA	-10.082 (± 2.4784)	-27.849 (± 11.3061)		
PALFTMS	2.574 (± 0.6833)	3.105 (± 2.0766)		

### Statistical analyses

Statistical analysis title	PALTEA
Comparison groups	Efficacy Analysis Set - CANTAB: UX007 v Efficacy Analysis Set - CANTAB: Placebo

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9378 <sup>[10]</sup>
Method	GEE model
Parameter estimate	Least squares mean difference
Point estimate	17.768
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.26
upper limit	36.79
Variability estimate	Standard error of the mean
Dispersion value	11.5659

Notes:

[10] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

<b>Statistical analysis title</b>	PALFTMS
Comparison groups	Efficacy Analysis Set - CANTAB: UX007 v Efficacy Analysis Set - CANTAB: Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5959 <sup>[11]</sup>
Method	GEE model
Parameter estimate	Least squares mean difference
Point estimate	-0.531
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.13
upper limit	3.06
Variability estimate	Standard error of the mean
Dispersion value	2.1853

Notes:

[11] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

### **Secondary: Change From Baseline to Week 8 in CANTAB, Spatial Span (SSP) Span Length Scores, GEE**

End point title	Change From Baseline to Week 8 in CANTAB, Spatial Span (SSP) Span Length Scores, GEE
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. SSP Span Length (SSPSLF) assesses the cognitive domain of sequential memory, with scores on a discrete, ordinal scale from 2 to 9; higher scores indicate better function. GEE statistical model.	
End point type	Secondary
End point timeframe: Baseline, Week 8	

End point values	Efficacy Analysis Set - CANTAB: UX007	Efficacy Analysis Set - CANTAB: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: units on a scale				
least squares mean (standard error)	0.019 ( $\pm$ 0.2387)	-0.041 ( $\pm$ 0.4246)		

## Statistical analyses

Statistical analysis title	SSPSLF
Comparison groups	Efficacy Analysis Set - CANTAB: Placebo v Efficacy Analysis Set - CANTAB: UX007
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4522 <sup>[12]</sup>
Method	GEE model
Parameter estimate	LS Mean Difference
Point estimate	0.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.76
upper limit	0.88
Variability estimate	Standard error of the mean
Dispersion value	0.4988

Notes:

[12] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

## Secondary: Change From Baseline to Week 8 in CANTAB, Spatial Working Memory (SWM) Scores, GEE

End point title	Change From Baseline to Week 8 in CANTAB, Spatial Working Memory (SWM) Scores, GEE
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. SWM between errors (SWMBE48) assesses the cognitive domain of working memory, with scores on a discrete, ordinal scale from 0 to 360; lower scores indicate better function. SWM strategy (SWMS68) assesses the cognitive domain of executive function/strategy, with scores on a discrete, ordinal scale from 4 to 28; lower scores indicate better function. GEE statistical model.	
End point type	Secondary
End point timeframe:	
Baseline, Week 8	

<b>End point values</b>	Efficacy Analysis Set - CANTAB: UX007	Efficacy Analysis Set - CANTAB: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	11		
Units: units on a scale				
least squares mean (standard error)				
SWMBE48	1.003 ( $\pm$ 1.4582)	2.240 ( $\pm$ 1.8036)		
SWMS68	0.060 ( $\pm$ 0.4794)	0.022 ( $\pm$ 0.4279)		

### Statistical analyses

<b>Statistical analysis title</b>	SWMBE48
Comparison groups	Efficacy Analysis Set - CANTAB: UX007 v Efficacy Analysis Set - CANTAB: Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3017 <sup>[13]</sup>
Method	GEE model
Parameter estimate	LS Mean Difference
Point estimate	-1.237
Confidence interval	
level	90 %
sides	2-sided
lower limit	-5.15
upper limit	2.68
Variability estimate	Standard error of the mean
Dispersion value	2.381

Notes:

[13] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

<b>Statistical analysis title</b>	SWMS68
Comparison groups	Efficacy Analysis Set - CANTAB: UX007 v Efficacy Analysis Set - CANTAB: Placebo
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5235 <sup>[14]</sup>
Method	GEE model
Parameter estimate	LS Mean Difference
Point estimate	0.038

Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.03
upper limit	1.11
Variability estimate	Standard error of the mean
Dispersion value	0.6495

Notes:

[14] - One-sided p-value. Additional model covariates include the corresponding baseline CANTAB score, visit and the interaction between visit and treatment.

## Secondary: Change From Baseline to Week 8 in Distance Traveled (in Meters) as Measured by 6-Minute Walk Test (6MWT)

End point title	Change From Baseline to Week 8 in Distance Traveled (in Meters) as Measured by 6-Minute Walk Test (6MWT)
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End point description:

Subjects were instructed to walk the length of a pre-measured 20-30 meter course in a hallway for 6 consecutive minutes. The total distance walked (meters) in a 6 minute period was recorded.

End point type	Secondary
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End point timeframe:

Baseline, Week 8

End point values	Efficacy Analysis Set – 6MWT: UX007	Efficacy Analysis Set – 6MWT: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	11		
Units: meters				
least squares mean (standard error)	-10.336 (± 14.8614)	-3.439 (± 16.1506)		

## Statistical analyses

Statistical analysis title	6MWT distance traveled
Comparison groups	Efficacy Analysis Set – 6MWT: UX007 v Efficacy Analysis Set – 6MWT: Placebo
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6205 <sup>[15]</sup>
Method	GEE model
Parameter estimate	LS Mean Difference
Point estimate	-6.897
Confidence interval	
level	90 %
sides	2-sided
lower limit	-43.874
upper limit	30.08

Variability estimate	Standard error of the mean
Dispersion value	22.4806

Notes:

[15] - One-sided p-value. Additional model covariates include the corresponding baseline value, visit and the interaction between visit and treatment.

### Secondary: Change From Baseline to Week 8 in Distance Traveled (in Percent Predicted) as Measured by 6MWT

End point title	Change From Baseline to Week 8 in Distance Traveled (in Percent Predicted) as Measured by 6MWT
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End point description:

Subjects were instructed to walk the length of a pre-measured 20-30 meter course in a hallway for 6 consecutive minutes. The total distance walked (meters) in a 6 minute period was recorded. The percent of predicted normal distance walked was determined based on published normative data.

End point type	Secondary
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End point timeframe:

Baseline, Week 8

End point values	Efficacy Analysis Set – 6MWT: UX007	Efficacy Analysis Set – 6MWT: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	11		
Units: percent predicted distance (in meters)				
least squares mean (standard error)	-1.338 (± 2.4752)	0.016 (± 2.6398)		

### Statistical analyses

<b>Statistical analysis title</b>	6MWT distance traveled (percent predicted)
Comparison groups	Efficacy Analysis Set – 6MWT: UX007 v Efficacy Analysis Set – 6MWT: Placebo
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6476 <sup>[16]</sup>
Method	GEE model
Parameter estimate	LS Mean Difference
Point estimate	-1.354
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.236
upper limit	4.527
Variability estimate	Standard error of the mean
Dispersion value	3.5759

Notes:

[16] - One-sided p-value. Additional model covariates include the corresponding baseline value, visit and the interaction between visit and treatment.

### Secondary: Time (in Minutes) to Onset of Paroxysmal Exertional Dyskinesia (PED) as Measured During 6MWT Over Time Through Week 8

End point title	Time (in Minutes) to Onset of Paroxysmal Exertional Dyskinesia (PED) as Measured During 6MWT Over Time Through Week 8
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End point description:

For the 6MWT, subjects were instructed to walk the length of a pre-measured 20-30 meter course in a hallway for 6 consecutive minutes. The total distance walked (meters) in a 6 minute period was recorded. PED occurring during the 6MWT was assessed. (PED is characterized by transient abnormal, involuntary movements primarily affecting the legs and feet, and typically precipitated by prolonged exertion.)

End point type	Secondary
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End point timeframe:

Baseline, Week 4, Week 8

End point values	Efficacy Analysis Set – 6MWT: UX007	Efficacy Analysis Set – 6MWT: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3 <sup>[17]</sup>	0 <sup>[18]</sup>		
Units: minutes				
arithmetic mean (standard deviation)				
Week 4	4.7 (± 4.73)	( )		
Week 8	1.8 (± 1.30)	( )		

Notes:

[17] - subjects with at least 1 PED

[18] - subjects with at least 1 PED

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline to Week 8 in Gross Motor Function Measure-88 (GMFM-88) Total Score

End point title	Change From Baseline to Week 8 in Gross Motor Function Measure-88 (GMFM-88) Total Score
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End point description:

The GMFM-88 is a standardized observational measure of abilities that includes the following 5 domains: lying/rolling, sitting, crawling/kneeling, standing, and walking/running/jumping. The GMFM-88 scores include the following:

- Lying & Rolling Score, Range 0–100%, higher is better
- Sitting Score, Range 0–100%, higher is better
- Crawling & Kneeling Score, Range 0–100%, higher is better
- Standing Score, Range 0–100%, higher is better
- Walking, Running & Jumping Score, Range 0–100%, higher is better
- Total Score = (Sum of 5 Above Scores) / 5, Range 0–100%, higher is better.

End point type	Secondary
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End point timeframe:

Baseline, Week 8

End point values	Efficacy Analysis Set - GMFM-88: UX007	Efficacy Analysis Set - GMFM-88: Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	11		
Units: score on a scale				
least squares mean (standard error)	3.209 ( $\pm$ 2.3669)	1.642 ( $\pm$ 2.6690)		

## Statistical analyses

<b>Statistical analysis title</b>	GMFM-88 UX007-Placebo
Comparison groups	Efficacy Analysis Set - GMFM-88: UX007 v Efficacy Analysis Set - GMFM-88: Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3435 <sup>[19]</sup>
Method	GEE model
Parameter estimate	LS Mean Difference
Point estimate	1.568
Confidence interval	
level	90 %
sides	2-sided
lower limit	-4.83
upper limit	7.97
Variability estimate	Standard error of the mean
Dispersion value	3.8899

Notes:

[19] - One-sided p-value. Additional model covariates include baseline GMFM-88 total score, visit and the interaction between visit and treatment.

## Secondary: Percent Reduction from Baseline Over Time in Frequency of Total Seizures (Normalized to a 4-Week Rate)

End point title	Percent Reduction from Baseline Over Time in Frequency of Total Seizures (Normalized to a 4-Week Rate)
End point description:	
Seizure frequency is based on observable seizures from the diary (normalized to a 4-week rate). Observable seizures from the diary include generalized tonic-clonic, generalized tonic, generalized clonic, generalized atonic, partial/focal with secondary generalization, myoclonic, myoclonic atonic, myoclonic tonic, complex partial/focal, simple partial/focal motor and absence seizures. Absence seizures from EEG include absence awake ( $\geq$ 10 sec), absence sleep ( $\geq$ 10 sec), indeterminate absence awake (3-10 sec), and indeterminate absence sleep (3-10 sec).	
End point type	Secondary
End point timeframe:	
Baseline, Week 26, Week 31	



End point values	UX007	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25 <sup>[20]</sup>	11 <sup>[21]</sup>		
Units: percent reduction of total seizures				
median (full range (min-max))				
Week 26; n= 22, 11	7.8 (-409 to 100)	0.0 (-207 to 94)		
Week 31; n=19, 8	42.7 (-267 to 100)	5.3 (-681 to 75)		

Notes:

[20] - n=subjects with an assessment at given time point

[21] - n=subjects with an assessment at given time point

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Reduction From Baseline Over Time in Frequency of Observable Seizures (Normalized to a 4-Week Rate)

End point title	Percent Reduction From Baseline Over Time in Frequency of Observable Seizures (Normalized to a 4-Week Rate)
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End point description:

Observable generalized and partial-onset seizures measured for 6 weeks by diary. Observable seizure frequency, the observable non-absence seizure frequency from the diary (normalized to a 4-week rate), is defined as Observable Seizure Frequency=Total number of seizures/Number of days observed×28. Seizure types include: Observable seizures from the diary include generalized tonic-clonic, generalized tonic, generalized clonic, generalized atonic, partial/focal with secondary generalization, myoclonic, myoclonic (astatic) atonic, myoclonic tonic, complex partial/focal, simple partial/focal motor, simple partial/focal sensory, and simple partial/focal psychological.

End point type	Secondary
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End point timeframe:

Baseline, Week 26, Week 31, Week 36, and Week 52

End point values	UX007	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17 <sup>[22]</sup>	10 <sup>[23]</sup>		
Units: percent reduction in observable seizures				
median (full range (min-max))				
Week 26; n=15, 10	0.0 (-260 to 88)	-27.7 (-207 to 74)		
Week 31; n=12, 7	23.6 (-267 to 100)	0.0 (-681 to 67)		
Week 36; n=12, 7	42.5 (-438 to 100)	-49.8 (-400 to 77)		
Week 52; n=12, 6	31.0 (-222 to 100)	-10.3 (-358 to 85)		

Notes:

[22] - n=observable seizures subjects with an assessment at given time point

[23] - n=observable seizures subjects with an assessment at given time point

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percent Reduction From Baseline Over Time in Frequency of Absence Seizures (Normalized to a 4-week Rate)

End point title	Percent Reduction From Baseline Over Time in Frequency of Absence Seizures (Normalized to a 4-week Rate)
End point description: Absence seizures measured overnight by EEG. The absence seizure frequency from EEG (normalized to a 24-hour rate) is defined as Absence Seizure Frequency=Total number of absence seizures/Number of hours observed×24. Seizure types include: absence awake (≥10 sec), absence sleep (≥10 sec), indeterminate absence awake (3-10 sec), and indeterminate absence sleep (3-10 sec).	
End point type	Secondary
End point timeframe: Baseline, Week 26, Week 31	

End point values	UX007	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19 <sup>[24]</sup>	6 <sup>[25]</sup>		
Units: percent reduction in absence seizures				
median (full range (min-max))				
Week 26; n=14, 4	0.0 (-3135 to 100)	0.0 (0 to 94)		
Week 31; n=12, 3	0.0 (-3905 to 100)	0.0 (0 to 75)		

Notes:

[24] - n=absence seizures subjects with an assessment at given time point

[25] - n=absence seizures subjects with an assessment at given time point

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

up to Week 52 plus 30 days

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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### Reporting groups

Reporting group title	UX007
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Reporting group description:

Subjects randomized to receive UX007, entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period.

Following completion of the Week 8 study visit, subjects continued treatment with open-label UX007 at the 35% dose level for an additional 44 weeks (Weeks 8-52).

Reporting group title	Placebo
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Reporting group description:

Subjects randomized to receive placebo entered a 2-week dose titration period to achieve study drug treatment comprising up to 35% of total daily calories or to the maximum tolerated dose level and maintained at the 35% total daily calorie dose level for a 6-week treatment period. Following completion of the Week 8 study visit, subjects continued treatment with open-label UX007 at the 35% dose level for an additional 44 weeks (Weeks 8-52).

Serious adverse events	UX007	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 25 (12.00%)	0 / 11 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Subcutaneous Haematoma			
subjects affected / exposed	1 / 25 (4.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 25 (4.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status Epilepticus			

subjects affected / exposed	3 / 25 (12.00%)	0 / 11 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	UX007	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 25 (100.00%)	11 / 11 (100.00%)	
Investigations			
Weight Increased			
subjects affected / exposed	4 / 25 (16.00%)	1 / 11 (9.09%)	
occurrences (all)	4	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 25 (8.00%)	1 / 11 (9.09%)	
occurrences (all)	2	2	
Fall			
subjects affected / exposed	2 / 25 (8.00%)	1 / 11 (9.09%)	
occurrences (all)	3	1	
Head Injury			
subjects affected / exposed	1 / 25 (4.00%)	1 / 11 (9.09%)	
occurrences (all)	1	2	
Ligament Sprain			
subjects affected / exposed	0 / 25 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Lip Injury			
subjects affected / exposed	0 / 25 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Procedural Pain			
subjects affected / exposed	0 / 25 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Nervous system disorders			
Clonic Convulsion			
subjects affected / exposed	0 / 25 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	

Dizziness			
subjects affected / exposed	3 / 25 (12.00%)	0 / 11 (0.00%)	
occurrences (all)	7	0	
Headache			
subjects affected / exposed	5 / 25 (20.00%)	0 / 11 (0.00%)	
occurrences (all)	38	0	
Seizure			
subjects affected / exposed	2 / 25 (8.00%)	0 / 11 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 25 (16.00%)	3 / 11 (27.27%)	
occurrences (all)	5	3	
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	2 / 25 (8.00%)	0 / 11 (0.00%)	
occurrences (all)	2	0	
Abdominal Distension			
subjects affected / exposed	0 / 25 (0.00%)	1 / 11 (9.09%)	
occurrences (all)	0	1	
Abdominal Pain			
subjects affected / exposed	7 / 25 (28.00%)	1 / 11 (9.09%)	
occurrences (all)	28	13	
Abdominal Pain Upper			
subjects affected / exposed	9 / 25 (36.00%)	1 / 11 (9.09%)	
occurrences (all)	16	1	
Breath Odour			
subjects affected / exposed	0 / 25 (0.00%)	2 / 11 (18.18%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	6 / 25 (24.00%)	1 / 11 (9.09%)	
occurrences (all)	7	3	
Diarrhoea			
subjects affected / exposed	16 / 25 (64.00%)	7 / 11 (63.64%)	
occurrences (all)	55	45	
Eructation			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Flatulence</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 25 (0.00%)</p> <p>0</p> <p>3 / 25 (12.00%)</p> <p>3</p> <p>8 / 25 (32.00%)</p> <p>29</p> <p>16 / 25 (64.00%)</p> <p>43</p>	<p>1 / 11 (9.09%)</p> <p>1</p> <p>1 / 11 (9.09%)</p> <p>1</p> <p>0 / 11 (0.00%)</p> <p>0</p> <p>5 / 11 (45.45%)</p> <p>12</p>	
<p>Reproductive system and breast disorders</p> <p>Dysmenorrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 25 (8.00%)</p> <p>3</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Epistaxis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Oropharyngeal Pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rhinorrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 25 (4.00%)</p> <p>1</p> <p>2 / 25 (8.00%)</p> <p>3</p> <p>1 / 25 (4.00%)</p> <p>2</p> <p>1 / 25 (4.00%)</p> <p>1</p>	<p>2 / 11 (18.18%)</p> <p>2</p> <p>0 / 11 (0.00%)</p> <p>0</p> <p>1 / 11 (9.09%)</p> <p>1</p> <p>1 / 11 (9.09%)</p> <p>1</p>	
<p>Skin and subcutaneous tissue disorders</p> <p>Acne</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 25 (8.00%)</p> <p>2</p>	<p>0 / 11 (0.00%)</p> <p>0</p>	
<p>Psychiatric disorders</p> <p>Abnormal Behaviour</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 25 (8.00%)</p> <p>2</p>	<p>1 / 11 (9.09%)</p> <p>1</p>	

Agitation subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 4	0 / 11 (0.00%) 0	
Confusional State subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 11 (9.09%) 3	
Insomnia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	1 / 11 (9.09%) 1	
Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	1 / 11 (9.09%) 1	
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 11 (9.09%) 1	
Gastroenteritis Viral subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	1 / 11 (9.09%) 1	
Gastrointestinal Viral Infection subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 11 (9.09%) 1	
Influenza subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 11 (9.09%) 1	
Otitis Media Acute subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 11 (9.09%) 1	
Sinusitis subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	1 / 11 (9.09%) 1	
Staphylococcal Infection subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 11 (9.09%) 1	
Upper Respiratory Tract Infection			

subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 4	2 / 11 (18.18%) 2	
Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	5 / 25 (20.00%) 10	2 / 11 (18.18%) 2	
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	5 / 25 (20.00%) 5	2 / 11 (18.18%) 2	



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2013	<ol style="list-style-type: none"><li>1. Study Sites. The number of study sites was increased.</li><li>2. Number of Subjects Planned was increased.</li><li>3. Study Procedures and Assessments were modified.</li><li>4. Primary Efficacy Hypothesis was modified.</li><li>5. The primary objective language was modified.</li><li>6. Inclusion Criteria was modified.</li><li>7. Treatment Administration: A recommended dose titration schedule was inserted. In addition, dose administration guidelines were modified.</li><li>8. Drug Concentration Measurements for population PK assessments were modified.</li><li>9. Suicidal Ideation and Behavior Assessments were modified.</li><li>10. Statistical Methods plans were modified.</li></ol>
20 May 2014	<ol style="list-style-type: none"><li>1. Number of Subjects Planned was revised.</li><li>2. Primary Efficacy Hypothesis was modified.</li><li>3. Study Objectives were modified or added to Section 6 in order to align study objectives with modifications to study design and endpoints.</li><li>4. Overall Study Design and Plan was modified.</li><li>5. Inclusion Criteria was modified.</li><li>6. Study Procedures and Assessments were modified</li><li>7. Efficacy Measures were changed.</li><li>8. Drug Concentration Measurements were modified.</li><li>9. Statistical Analysis &amp; Determination of Sample Size was updated.</li></ol>
09 December 2014	<ol style="list-style-type: none"><li>1. The adaptive study design component of the protocol was eliminated.</li><li>2. Inclusion criteria were updated, changed, and/or removed.</li><li>3. The primary and secondary objectives of the study were updated and the primary and secondary endpoints were updated to reflect the changes to the objectives to include a more robust evaluation of triheptanoin in patients with absence seizures.</li><li>4. The randomization was changed from 1:1 to 3:1 (UX007: placebo).</li><li>5. An EEG assessment was added at the Screening Visit.</li><li>6. Removal of Subjects from Therapy or Assessment was updated to clarify the conditions under which subjects either will be removed or may be removed from study participation.</li></ol>
30 November 2015	<ol style="list-style-type: none"><li>1. Edited Inclusion Criteria.</li><li>2. Updated the list of excluded medications.</li><li>3. Primary objective changed to 'Evaluate the efficacy of UX007 compared to placebo as measured by the reduction from randomization to week 8 in frequency of seizures'.</li><li>4. The EEG at Screening for patients with absence seizures only was required for ~3 hours, not overnight.</li><li>5. The Erythrocyte Glucose Uptake Assay was removed from the protocol.</li><li>6. Plasma level sample collection range for the population PK study at Week 26 was changed from 30 – 180 minutes to 60 and 180 minutes.</li></ol>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported