Clinical trial results:
An Open-label Long-Term Safety and Efficacy Extension Study in Subjects with Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD) Previously Enrolled in UX007 or Triheptanoin Studies

Summary

EudraCT number	2016-000322-19
Trial protocol	GB
Global end of trial date	03 December 2020

Results information

Result version number	v2 (current)
This version publication date	22 July 2022
First version publication date	27 October 2021
Version creation reason	• Correction of full data set revised study completion date

Trial information

Trial identification

Sponsor protocol code	UX007-CL202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02214160
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 8887568567, medinfo@ultragenyx.com
Scientific contact	Medical Information, Ultragenyx Pharmaceutical Inc., 1 8887568567, 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	03 December 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the long-term safety and efficacy of UX007 in participants with LC-FAOD. The secondary objectives of this study are to evaluate the effect of UX007 on energy metabolism in LC-FAOD and evaluate the impact of UX007 on clinical events associated with LC-FAOD.

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	09 December 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 88
Country: Number of subjects enrolled	United Kingdom: 6
Worldwide total number of subjects	94
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	7
Children (2-11 years)	47
Adolescents (12-17 years)	16
Adults (18-64 years)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included LC-FAOD subjects who have participated in prior clinical studies or treatment programs with UX007/triheptanoin, or who had failed conventional therapy and had documented clear unmet need (in the opinion of the Investigator and Sponsor).

Period 1

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

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	UX007-CL201-Rollover Cohort

Arm description:

Participants who participated in the UX007-CL201 study (NCT01886378) receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Arm type	Experimental
Investigational medicinal product name	Triheptanoin
Investigational medicinal product code	UX007
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Triheptanoin was administered orally (PO) with food or by gastronomy tube (usually four times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Arm title	IST/Other Cohort

Arm description:

Participants who were previously treated with UX007/triheptanoin (including food-grade triheptanoin) in an investigator sponsored trial (IST) or another UX007/triheptanoin study receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Arm type	Experimental
Investigational medicinal product name	Triheptanoin
Investigational medicinal product code	UX007
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Triheptanoin was administered orally (PO) with food or by gastronomy tube (usually four times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Arm title	Triheptanoin-Naïve Cohort

Arm description:

Participants who are UX007 treatment-naïve (i.e., naïve to both UX007 and food-grade triheptanoin), or who had failed conventional therapy (including those who participated in UX007-CL201 study previously

but were off UX007 for more than 2 years preceding enrollment into CL202) receive UX007, administered orally with food or
by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Arm type	Experimental
Investigational medicinal product name	Triheptanoin
Investigational medicinal product code	UX007
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Triheptanoin was administered orally (PO) with food or by gastronomy tube (usually four times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Number of subjects in period 1	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort
Started	24	37	33
Completed	20	29	23
Not completed	4	8	10
Consent withdrawn by subject	1	-	6
Adverse Event	-	1	1
Physician Decision	-	-	1
Death	2	2	1
Subject Non- Compliance	-	3	1
Sponsor Decision	-	2	-
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	UX007-CL201-Rollover Cohort
Reporting group description:	
Participants who participated in the UX007-CL201 study (NCT01886378) receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.	
Reporting group title	IST/Other Cohort
Reporting group description:	
Participants who were previously treated with UX007/triheptanoin (including food-grade triheptanoin) in an investigator sponsored trial (IST) or another UX007/triheptanoin study receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.	
Reporting group title	Triheptanoin-Naïve Cohort
Reporting group description:	
Participants who are UX007 treatment-naïve (i.e., naïve to both UX007 and food-grade triheptanoin), or who had failed conventional therapy (including those who participated in UX007-CL201 study previously but were off UX007 for more than 2 years preceding enrollment into CL202) receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.	

Reporting group values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort
Number of subjects	24	37	33
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	13.16	17.69	9.33
standard deviation	± 14.310	± 14.490	± 9.745
Gender categorical Units: Subjects			
Female	10	21	14
Male	14	16	19
Ethnicity Units: Subjects			
Hispanic or Latino	3	4	5
Not Hispanic or Latino	21	30	28
Unknown or Not Reported	0	3	0
Race Units: Subjects			
Asian	1	1	1
Black or African American	1	1	2
White	21	33	28
Other, Not Specified	1	2	2

Reporting group values	Total		
Number of subjects	94		

Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	45		
Male	49		
Ethnicity Units: Subjects			
Hispanic or Latino	12		
Not Hispanic or Latino	79		
Unknown or Not Reported	3		
Race Units: Subjects			
Asian	3		
Black or African American	4		
White	82		
Other, Not Specified	5		

End points

End points reporting groups

Reporting group title	UX007-CL201-Rollover Cohort

Reporting group description:

Participants who participated in the UX007-CL201 study (NCT01886378) receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Reporting group title	IST/Other Cohort

Reporting group description:

Participants who were previously treated with UX007/triheptanoin (including food-grade triheptanoin) in an investigator sponsored trial (IST) or another UX007/triheptanoin study receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Reporting group title	Triheptanoin-Naïve Cohort

Reporting group description:

Participants who are UX007 treatment-naïve (i.e., naïve to both UX007 and food-grade triheptanoin), or who had failed conventional therapy (including those who participated in UX007-CL201 study previously but were off UX007 for more than 2 years preceding enrollment into CL202) receive UX007, administered orally with food or
by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Primary: Annualized LC-FAOD Major Clinical Events (MCEs) Rate: 18 Months Pre- and Entire UX007 Period Comparison for UX007-CL201-Rollover Cohort

End point title	Annualized LC-FAOD Major Clinical Events (MCEs) Rate: 18 Months Pre- and Entire UX007 Period Comparison for UX007-CL201-Rollover Cohort[1][2]

End point description:

The annualized LC-FAOD MCE rate, inclusive of skeletal myopathy (rhabdomyolysis), hepatic (hypoglycemia) and cardiomyopathy events, defined as any visit to the emergency room (ER)/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LC-FAOD.
The annualized event rate was calculated at the number of events divided by the duration of data collection period in days/365.25

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Primary

End point timeframe:

Pre-UX007 treatment period (up to 18 months) and post-UX007 treatment period (up to 2072 days)

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: Statistics are presented in the data table per protocol.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are presented in the data table per protocol.

End point values	UX007-CL201-Rollover Cohort			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: events/year				
arithmetic mean (standard deviation)				
Pre-UX007 Period	1.76 (± 1.64)			
UX007 Treatment Period	1.00 (± 1.00)			

Attachments (see zip file)	OM1 stat analysis.docx

Statistical analyses

No statistical analyses for this end point

Primary: Annualized LC-FAOD MCEs Rate: 18 Months Pre- and Entire UX007 Period Comparison for IST/Other Cohort and Triheptanoin-Naïve Cohort

End point title	Annualized LC-FAOD MCEs Rate: 18 Months Pre- and Entire UX007 Period Comparison for IST/Other Cohort and Triheptanoin-Naïve Cohort[3][4]

End point description:

The annualized LC-FAOD MCE rate, inclusive of skeletal myopathy (rhabdomyolysis), hepatic (hypoglycemia) and cardiomyopathy events, defined as any visit to the emergency room (ER)/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LC-FAOD.
The annualized event rate was calculated at the number of events divided by the duration of data collection period in days/365.25.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. Per protocol, pre-UX007 MCE data was not collected in the IST/Other Cohort.

End point type	Primary

End point timeframe:

Pre-UX007 treatment period (up to 18 months) and post-UX007 treatment period (up to 2072 days)

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: Statistics are presented in the data table per protocol.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Statistics are presented in the data table per protocol.

End point values	IST/Other Cohort	Triheptanoin-Naïve Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[5]	33		
Units: events/year				
median (inter-quartile range (Q1-Q3))				
Pre-UX007 Period; n=0, 33	99999 (99999 to 99999)	2.00 (0.67 to 3.33)		
UX007 Treatment Period; n=37, 33	0.57 (0.0 to 1.67)	0.28 (0.00 to 1.43)		

Notes:

[5] - 99999=not collected (per protocol)

Attachments (see zip file)	OM2 stat analysis.docx

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) or Serious TEAEs

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs) or Serious TEAEs[6]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence, whether or not considered drug related. A serious adverse event (SAE) 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; a congenital anomaly/birth defect; an important medical event. AEs were graded using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 (mild=1, moderate=2, severe=3, life-threatening=4, death=5).

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

End point type	Primary

End point timeframe:

Post-UX007 treatment through the end of treatment (up to 2072 days) plus 30-35 days

Notes:

[6] - 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 in the data table per protocol.

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: participants				
>= 1 TEAE	24	35	32	
Treatment-Related TEAEs	14	22	28	
Treatment-Related Gastrointestinal (GI) TEAEs	10	19	27	
Grade 3 TEAEs	16	26	18	
Grade 4 TEAEs	3	2	2	
Serious TEAEs	20	28	22	
Treatment-Related Serious TEAEs	1	1	3	
TEAEs Leading to Treatment Discontinuation	1	1	1	
TEAEs Leading to Study Discontinuation	0	1	1	
TEAEs Leading to Death	2	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Echocardiogram (ECHO) Parameters Over Time: Left Ventricular Mass Index (LVMI)

End point title	Change From Baseline in Echocardiogram (ECHO) Parameters Over Time: Left Ventricular Mass Index (LVMI)

End point description:

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. n=participants with a value at baseline and given time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 24, Month 36, Month 48, Month 60

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[7]	37	33[8]	
Units: g/m				
arithmetic mean (standard deviation)				
Change at Month 12; n=15, 29, 16	-5.27 (± 21.433)	4.55 (± 21.903)	-9.06 (± 29.965)	
Change at Month 24; n=11, 27, 9	-2.73 (± 23.711)	-0.37 (± 18.132)	1.00 (± 39.459)	
Change at Month 36; n=12, 26, 6	-6.75 (± 28.933)	1.23 (± 19.488)	12.33 (± 38.831)	
Change at Month 48; n= 3, 23, 3	-12.33 (± 29.263)	-1.04 (± 21.900)	-9.67 (± 36.529)	
Change at Month 60; n=0, 6, 0	99999 (± 99999)	8.83 (± 25.639)	99999 (± 99999)	

Notes:

[7] - 99999=0 participants analyzed at this time point

[8] - 99999=0 participants analyzed at this time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ECHO Parameters Over Time: Left Ventricular Mass Index (LVM)

End point title	Change From Baseline in ECHO Parameters Over Time: Left Ventricular Mass Index (LVM)

End point description:

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. Participants with a value at baseline and given time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 24, Month 36, Month 48, Month 60

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[9]	37	33[10]	
Units: grams				
arithmetic mean (standard deviation)				
Change at Month 12; n=18, 31, 20	-1.50 (± 29.374)	12.58 (± 22.648)	-0.75 (± 25.935)	
Change at Month 24; n=17, 28, 12	9.71 (± 27.034)	5.61 (± 34.465)	3.25 (± 38.833)	
Change at Month 36; n=14, 28, 8	6.21 (± 30.355)	16.36 (± 36.898)	15.75 (± 48.922)	
Change at Month 48; n=4, 25, 4	33.25 (± 12.842)	19.72 (± 42.645)	10.25 (± 52.753)	
Change at Month 60; n=0, 7, 0	99999 (± 99999)	46.29 (± 19.102)	99999 (± 99999)	

Notes:

[9] - 99999=no participants at this time point.

[10] - 99999=no participants at this time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ECHO Parameters Over Time: Left Ventricular Diameter (LVD)

End point title	Change From Baseline in ECHO Parameters Over Time: Left Ventricular Diameter (LVD)

End point description:

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. Participants with a value at baseline and given time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 24, Month 36, Month 48, Month 60

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[11]	37	33[12]	
Units: mm				
arithmetic mean (standard deviation)				
Change at Month 12; n=18, 29, 21	2.19 (± 9.138)	2.38 (± 8.719)	1.57 (± 4.308)	
Change at Month 24; n=17, 27, 12	3.26 (± 11.158)	3.00 (± 8.535)	0.67 (± 4.755)	
Change at Month 36; n=17, 26, 9	-0.11 (± 13.174)	3.23 (± 8.883)	4.78 (± 5.094)	
Change at Month 48; n=4, 23, 5	10.88 (± 17.264)	3.82 (± 9.115)	2.60 (± 5.177)	
Change at Month 60; n=0, 7, 1	99999 (± 99999)	-5.00 (± 7.394)	50.00 (± 999999)	

Notes:

[11] - 99999=not applicable (0 participants)

[12] - 999999=not applicable (1 participant)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ECHO Parameters Over Time: Left Ventricular Ejection Fraction (LVEF)

End point title	Change From Baseline in ECHO Parameters Over Time: Left Ventricular Ejection Fraction (LVEF)

End point description:

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. Participants with a value at baseline and given time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 18, Month 24, Month 30, Month 36, Month 48, Month 60

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[13]	37[14]	33[15]	
Units: percent of blood ejected during systole				
arithmetic mean (standard deviation)				
Change at Month 12; n=21, 31, 21	0.76 (± 7.602)	1.32 (± 7.254)	0.71 (± 6.474)	
Change at Month 18; n=0, 0, 1	99999 (± 99999)	99999 (± 99999)	0.00 (± 999999)	
Change at Month 24; n=22, 25, 13	-1.86 (± 9.062)	0.24 (± 8.875)	2.31 (± 8.400)	
Change at Month 30; n=1, 0, 0	0.00 (± 999999)	99999 (± 99999)	99999 (± 99999)	
Change at Month 36; n=21, 26, 9	-1.10 (± 7.259)	-1.92 (± 5.986)	3.44 (± 7.601)	
Change at Month 48; n=6, 23, 5	-1.33 (± 3.445)	-1.57 (± 7.464)	1.60 (± 5.459)	
Change at Month 60; n=0, 7, 1	99999 (± 99999)	-5.00 (± 7.394)	1.00 (± 999999)	

Notes:

[13] - 99999=no participant at this time point; 999999=not applicable, 1 participant at this time point

[14] - 99999=no participant at this time point

[15] - 99999=no participant at this time point; 999999=not applicable, 1 participant at this time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ECHO Parameters Over Time: LVEF Z-Score (Pediatric Participants)

End point title	Change From Baseline in ECHO Parameters Over Time: LVEF Z-Score (Pediatric Participants)

End point description:

The Z-scores express the deviation (or how far away) the measure is from the mean LVEF based on the size or age of the pediatric participants:

Z-score=0 indicates the participant is exactly the same as the mean of the healthy general population.
Z-score=-1 indicates it's 1 standard deviation below the mean of the healthy population.
Z-score=+1 indicates it's 1 standard deviation above the mean.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. Pediatric participants with a value at baseline and given time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 24, Month 36

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5[16]	1[17]	8[18]	
Units: z score				
arithmetic mean (standard deviation)				
Change at Month 12; n=4, 1, 4	0.34 (± 1.229)	1.84 (± 999999)	0.21 (± 1.492)	
Change at Month 24; n=4, 1, 2	-0.05 (± 1.469)	2.28 (± 999999)	0.72 (± 1.103)	
Change at Month 36; n=0, 1, 1	99999 (± 99999)	-0.52 (± 999999)	-0.66 (± 999999)	

Notes:

[16] - 99999=no participants at this time point.

[17] - 999999=not applicable, 1 participant at this time point.

[18] - 999999=1 participant at this time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ECHO Parameters Over Time: Left Ventricular Shortening Fraction (LVSF)

End point title	Change From Baseline in ECHO Parameters Over Time: Left Ventricular Shortening Fraction (LVSF)

End point description:

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. Participants with a value at baseline and given time point.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 24, Month 30, Month 36, Month 48, Month 60

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[19]	37[20]	33[21]	
Units: % reduction in left ventricular diameter				
arithmetic mean (standard deviation)				
Change at Month 12; n=20, 32, 21	-1.30 (± 5.564)	-0.91 (± 6.468)	-1.48 (± 5.904)	

Change at Month 24; n=20, 29, 14	-1.90 (± 6.052)	1.03 (± 6.242)	-1.36 (± 7.967)	
Change at Month 30; n=1, 0, 0	-7.00 (± 999999)	99999 (± 99999)	99999 (± 99999)	
Change at Month 36; n=20, 28, 9	-0.10 (± 6.086)	0.25 (± 4.502)	1.11 (± 5.395)	
Change at Month 48; n=4, 25, 5	3.00 (± 4.320)	0.52 (± 4.501)	-0.60 (± 6.269)	
Change at Month 60; n=0, 7, 1	99999 (± 99999)	-0.57 (± 4.392)	0.00 (± 999999)	

Notes:

[19] - 999999=1 participant at this time point

[20] - 99999=no participants at this time point.

[21] - 99999=no participants at this time point.999999=not applicable; 1 participant at this time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in ECHO Parameters Over Time: LVSF Z-Score (Pediatric Participants)

End point title	Change From Baseline in ECHO Parameters Over Time: LVSF Z-Score (Pediatric Participants)

End point description:

The Z-scores express the deviation (or how far away) the measure is from the mean LVSF based on the size or age of the pediatric participants:

Z-score=0 indicates the participant is exactly the same as the mean of the healthy general population.
Z-score=-1 indicates it's 1 standard deviation below the mean of the healthy population.
Z-score=+1 indicates it's 1 standard deviation above the mean.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment. Pediatric participants with a value at baseline and given time
point.

End point type	Secondary

End point timeframe:

Baseline, Month 12, Month 24, Month 36, Month 48, Month 60

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24[22]	37	33[23]	
Units: z score				
arithmetic mean (standard deviation)				
Change at Month 12; n=11, 25, 14	0.10 (± 1.659)	0.25 (± 1.315)	-0.38 (± 1.597)	
Change at Month 24; n=11, 23, 9	0.27 (± 2.255)	0.30 (± 1.607)	0.13 (± 2.119)	
Change at Month 36; n=7, 23, 8	0.75 (± 1.729)	0.13 (± 1.115)	0.58 (± 1.943)	
Change at Month 48; n=3, 20, 5	0.53 (± 0.316)	0.24 (± 1.464)	0.10 (± 1.888)	
Change at Month 60; n=0, 6, 0	99999 (± 99999)	-0.45 (± 0.834)	99999 (± 99999)	

Notes:

[22] - 99999=no participants at this time point.

[23] - 99999=no participants at this time point.

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Duration Rate of All MCEs

End point title	Annualized Duration Rate of All MCEs

End point description:

The annualized duration rate of LC-FAOD MCEs, inclusive of skeletal myopathy (rhabdomyolysis), hepatic (hypoglycemia) and cardiomyopathy events, and defined as any visit to the ER/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LC-FAOD. The annualized duration rate is calculated as the total duration (days) of events divided by the duration of data collection period in days/365.25.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Post-UX007 treatment through the end of the study (up to 2072 days)

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: days/year				
median (inter-quartile range (Q1-Q3))	2.123 (0.000 to 9.766)	2.487 (0.000 to 6.968)	0.796 (0.000 to 5.484)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Event Rate of Rhabdomyolysis MCEs

End point title	Annualized Event Rate of Rhabdomyolysis MCEs

End point description:

The annualized event rate of LC-FAOD major events of skeletal myopathy (rhabdomyolysis), defined as any visit to the ER/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LCFAOD.
The annualized event rate was calculated at the number of events divided by the duration of data collection period in days/365.25.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Post-UX007 treatment through the end of the study (up to 2072 days)

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: events/year				
median (inter-quartile range (Q1-Q3))	0.352 (0.000 to 1.472)	0.574 (0.000 to 1.673)	0.281 (0.000 to 1.425)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Duration Rate of Rhabdomyolysis MCEs

End point title	Annualized Duration Rate of Rhabdomyolysis MCEs

End point description:

The annualized duration rate of LC-FAOD skeletal myopathy (rhabdomyolysis) MCEs, defined as any visit to the ER/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LCFAOD.
The annualized duration rate is calculated as the total duration (days) of events divided by the duration of data collection period in days/365.25.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Post-UX007 treatment through the end of the study (up to 2072 days)

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: days/year				
median (inter-quartile range (Q1-Q3))	2.123 (0.000 to 6.969)	2.487 (0.000 to 6.948)	0.448 (0.000 to 5.398)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Event Rate of Cardiomyopathy MCEs

End point title	Annualized Event Rate of Cardiomyopathy MCEs

End point description:

The annualized event rate of LC-FAOD major events inclusive of cardiomyopathy events, defined as any visit to the ER/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LCFAOD.
The annualized event rate was calculated at the number of events divided by the duration of data collection period in days/365.25.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Post-UX007 treatment through the end of the study (up to 2072 days)

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: event/year				
median (inter-quartile range (Q1-Q3))	0.000 (0.000 to 0.120)	0.000 (0.000 to 0.000)	0.000 (0.000 to 0.000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Duration Rate of Cardiomyopathy MCEs

End point title	Annualized Duration Rate of Cardiomyopathy MCEs

End point description:

The annualized duration rate of LC-FAOD cardiomyopathy MCEs, defined as any visit to the ER/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LC-FAOD.
The annualized duration rate is calculated as the total duration (days) of events divided by the duration of data collection period in days/365.25

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Post-UX007 treatment through the end of the study (up to 2072 days

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: days/year				
median (inter-quartile range (Q1-Q3))	0.000 (0.000 to 0.174)	0.000 (0.000 to 0.000)	0.000 (0.000 to 0.000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Event Rate of Hypoglycemic MCEs

End point title	Annualized Event Rate of Hypoglycemic MCEs

End point description:

The annualized event rate of LC-FAOD major events of hepatic (hypoglycemia) events, defined as any visit to the ER/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LCFAOD.
The annualized event rate was calculated at the number of events divided by the duration of data collection period in days/365.25.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Post-UX007 treatment through the end of the study (up to 2072 days)

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: events/year				
median (inter-quartile range (Q1-Q3))	0.000 (0.000 to 0.000)	0.000 (0.000 to 0.000)	0.000 (0.000 to 0.000)	

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Duration Rate of Hypoglycemic MCEs

End point title	Annualized Duration Rate of Hypoglycemic MCEs

End point description:

The annualized duration rate of LC-FAOD hepatic (hypoglycemia) MCEs, defined as any visit to the ER/acute care, hospitalization, emergency intervention (i.e. any unscheduled administration of therapeutics at home or in the clinic), or any similar event whether caused primarily by LC-FAOD or by an intercurrent illness complicated by LC-FAOD.
The annualized duration rate is calculated as the total duration (days) of events divided by the duration of data collection period in days/365.25.

Full Analysis Set: all participants enrolled who had at least 1 post-baseline efficacy assessment.

End point type	Secondary

End point timeframe:

Post-UX007 treatment through the end of the study (up to 2072 days)

End point values	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	37	33	
Units: days/year				
median (inter-quartile range (Q1-Q3))	0.000 (0.000 to 0.000)	0.000 (0.000 to 0.000)	0.000 (0.000 to 0.000)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Post-UX007 treatment through the end of treatment (up to 2072 days) plus 30-35 days

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	UX007-CL201- Rollover Cohort

Reporting group description:

Participants who participated in the UX007-CL201 study (NCT01886378) receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Reporting group title	IST/Other Cohort

Reporting group description:

Participants who were previously treated with UX007/triheptanoin (including food-grade triheptanoin) in an investigator sponsored trial (IST) or another UX007/triheptanoin study receive UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Reporting group title	Triheptanoin-Naïve Cohort

Reporting group description:

Participants who are UX007 treatment-naïve (i.e., naïve to both UX007 and food-grade triheptanoin), or who had failed conventional therapy (including those who participated in UX007-CL201 study previously but were off UX007 for more than 2 years preceding enrollment into CL202) receive UX007, administered orally with food or
by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the target dose range of 25-35% of total calories.

Reporting group title	All Participants

Reporting group description:

All participants received UX007, administered orally with food or by gastronomy tube (usually 4 times per day: breakfast, lunch, dinner, and before bed), at the
target dose range of 25-35% of total calories.

Serious adverse events	UX007-CL201- Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 24 (83.33%)	28 / 37 (75.68%)	22 / 33 (66.67%)
number of deaths (all causes)	2	2	1
number of deaths resulting from adverse events	2	2	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
PLEOMORPHIC ADENOMA			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
Vascular disorders			

HAEMODYNAMIC INSTABILITY			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
POOR VENOUS ACCESS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
Surgical and medical procedures			
ELECTIVE PROCEDURE			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
HEART TRANSPLANT			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
CHRONIC RESPIRATORY FAILURE			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
PULMONARY OEDEMA			

subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	2 / 24 (8.33%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
TONSILLAR HYPERTROPHY			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
LISTLESS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
Investigations			
AMMONIA INCREASED			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

BRAIN NATRIURETIC PEPTIDE INCREASED			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
INFLUENZA A VIRUS TEST POSITIVE			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
OVERDOSE			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
PROCEDURAL PAIN			
subjects affected / exposed	1 / 24 (4.17%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ARRHYTHMIA			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
CARDIAC ARREST			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE			

subjects affected / exposed	2 / 24 (8.33%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
CARDIAC FAILURE ACUTE			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
CARDIOMYOPATHY			
subjects affected / exposed	4 / 24 (16.67%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CARDIOPULMONARY FAILURE			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONGESTIVE CARDIOMYOPATHY			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEFT VENTRICULAR HYPERTROPHY			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
LONG QT SYNDROME			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
MYOCARDITIS			

subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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			
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
HEADACHE			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LETHARGY			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POLYNEUROPATHY			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
SEIZURE			

subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
Gastrointestinal disorders			
CHRONIC GASTRITIS			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC ULCER HAEMORRHAGE			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
GASTRITIS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
GASTROINTESTINAL DISORDER			
subjects affected / exposed	3 / 24 (12.50%)	6 / 37 (16.22%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 4	0 / 9	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			

subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL POLYP			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
STEATORRHOEA			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
VOLVULUS			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
VOMITING			
subjects affected / exposed	2 / 24 (8.33%)	4 / 37 (10.81%)	5 / 33 (15.15%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	2 / 24 (8.33%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL FAILURE			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
JOINT INSTABILITY			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

MYALGIA			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
OSTEOPOROSIS			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 24 (4.17%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHABDOMYOLYSIS			
subjects affected / exposed	14 / 24 (58.33%)	25 / 37 (67.57%)	15 / 33 (45.45%)
occurrences causally related to treatment / all	0 / 64	0 / 179	2 / 49
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SCOLIOSIS			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
Infections and infestations			
CELLULITIS			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
CROUP INFECTIOUS			
subjects affected / exposed	1 / 24 (4.17%)	1 / 37 (2.70%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			

subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
DIVERTICULITIS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
GASTRITIS VIRAL			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
GASTROENTERITIS			
subjects affected / exposed	5 / 24 (20.83%)	5 / 37 (13.51%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS VIRAL			
subjects affected / exposed	4 / 24 (16.67%)	3 / 37 (8.11%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 6	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL VIRAL INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES SIMPLEX			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			

subjects affected / exposed	2 / 24 (8.33%)	8 / 37 (21.62%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 3	0 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KLEBSIELLA BACTERAEMIA			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KLEBSIELLA INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	1 / 24 (4.17%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA STAPHYLOCOCCAL			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
PYELONEPHRITIS			

subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RHINOVIRUS INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLITIS			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
TRACHEITIS			

subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 24 (8.33%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
VIRAL CARDIOMYOPATHY			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (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
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 24 (8.33%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
ACIDOSIS			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	3 / 24 (12.50%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERAMMONAEMIA			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			

subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
HYPOPHAGIA			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	0 / 33 (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
METABOLIC DISORDER			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	All Participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	70 / 94 (74.47%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	5		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
PLEOMORPHIC ADENOMA			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
HAEMODYNAMIC INSTABILITY			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
POOR VENOUS ACCESS			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
ELECTIVE PROCEDURE			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEART TRANSPLANT			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CHRONIC RESPIRATORY FAILURE			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PULMONARY OEDEMA			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
RESPIRATORY DISTRESS			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY FAILURE			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		

TONSILLAR HYPERTROPHY				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
ANXIETY				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LISTLESS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
AMMONIA INCREASED				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
BLOOD CREATINE PHOSPHOKINASE INCREASED				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
BRAIN NATRIURETIC PEPTIDE INCREASED				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INFLUENZA A VIRUS TEST POSITIVE				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
TRANSAMINASES INCREASED				

subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
OVERDOSE			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PROCEDURAL PAIN			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
ARRHYTHMIA			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC ARREST			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
CARDIAC FAILURE			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 2		
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

CARDIOMYOPATHY				
subjects affected / exposed	5 / 94 (5.32%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 1			
CARDIOPULMONARY FAILURE				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
CONGESTIVE CARDIOMYOPATHY				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
LEFT VENTRICULAR HYPERTROPHY				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LONG QT SYNDROME				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
MYOCARDITIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
HAEMORRHAGE INTRACRANIAL				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HEADACHE				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ISCHAEMIC STROKE				

subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LETHARGY				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
MIGRAINE				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
NEUROPATHY PERIPHERAL				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
POLYNEUROPATHY				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
SEIZURE				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
CHRONIC GASTRITIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
DIARRHOEA				
subjects affected / exposed	4 / 94 (4.26%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
GASTRIC ULCER HAEMORRHAGE				

subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
GASTRITIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
GASTROINTESTINAL DISORDER				
subjects affected / exposed	11 / 94 (11.70%)			
occurrences causally related to treatment / all	0 / 17			
deaths causally related to treatment / all	0 / 0			
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
ILEUS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
PANCREATITIS ACUTE				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
RECTAL POLYP				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STEATORRHOEA				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VOLVULUS				

subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VOMITING				
subjects affected / exposed	11 / 94 (11.70%)			
occurrences causally related to treatment / all	0 / 13			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
ACUTE KIDNEY INJURY				
subjects affected / exposed	3 / 94 (3.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
RENAL FAILURE				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Musculoskeletal and connective tissue disorders				
JOINT INSTABILITY				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
MYALGIA				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OSTEOPOROSIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PAIN IN EXTREMITY				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

RHABDOMYOLYSIS			
subjects affected / exposed	54 / 94 (57.45%)		
occurrences causally related to treatment / all	2 / 292		
deaths causally related to treatment / all	0 / 1		
SCOLIOSIS			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
CELLULITIS			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CROUP INFECTIOUS			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DIVERTICULITIS			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

GASTRITIS VIRAL			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS			
subjects affected / exposed	12 / 94 (12.77%)		
occurrences causally related to treatment / all	0 / 15		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS VIRAL			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL VIRAL INFECTION			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HERPES SIMPLEX			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INFLUENZA			
subjects affected / exposed	11 / 94 (11.70%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 0		
KLEBSIELLA BACTERAEMIA			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
KLEBSIELLA INFECTION			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ORAL CANDIDIASIS			

subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PARAINFLUENZAE VIRUS INFECTION				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PHARYNGITIS STREPTOCOCCAL				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA STAPHYLOCOCCAL				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PYELONEPHRITIS				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY TRACT INFECTION VIRAL				
subjects affected / exposed	3 / 94 (3.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
RHINOVIRUS INFECTION				

subjects affected / exposed	2 / 94 (2.13%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
SEPSIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STAPHYLOCOCCAL BACTERAEMIA				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
STAPHYLOCOCCAL INFECTION				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TONSILLITIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TRACHEITIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	5 / 94 (5.32%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VIRAL CARDIOMYOPATHY				

subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
VIRAL UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	5 / 94 (5.32%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
ACIDOSIS				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
DEHYDRATION				
subjects affected / exposed	5 / 94 (5.32%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
HYPERAMMONAEMIA				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
HYPOKALAEMIA				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
HYPOPHAGIA				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
METABOLIC DISORDER				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	UX007-CL201-Rollover Cohort	IST/Other Cohort	Triheptanoin-Naïve Cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)	34 / 37 (91.89%)	32 / 33 (96.97%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 24 (4.17%)	6 / 37 (16.22%)	0 / 33 (0.00%)
occurrences (all)	1	6	0
POOR VENOUS ACCESS			
subjects affected / exposed	3 / 24 (12.50%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	3	0	0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	4	0
FATIGUE			
subjects affected / exposed	3 / 24 (12.50%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	3	4	1
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	2 / 24 (8.33%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	5	1	0
PAIN			
subjects affected / exposed	4 / 24 (16.67%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	6	2	0
PYREXIA			
subjects affected / exposed	9 / 24 (37.50%)	5 / 37 (13.51%)	5 / 33 (15.15%)
occurrences (all)	16	8	11
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
HYPERSENSITIVITY			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
SEASONAL ALLERGY			

subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	3 / 33 (9.09%)
occurrences (all)	0	1	3
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
COUGH			
subjects affected / exposed	6 / 24 (25.00%)	3 / 37 (8.11%)	6 / 33 (18.18%)
occurrences (all)	9	3	8
DYSPNOEA			
subjects affected / exposed	2 / 24 (8.33%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	2	3	1
HYPOXIA			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
NASAL CONGESTION			
subjects affected / exposed	4 / 24 (16.67%)	2 / 37 (5.41%)	3 / 33 (9.09%)
occurrences (all)	6	2	3
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 24 (8.33%)	3 / 37 (8.11%)	3 / 33 (9.09%)
occurrences (all)	2	3	3
RESPIRATORY DISORDER			
subjects affected / exposed	1 / 24 (4.17%)	9 / 37 (24.32%)	3 / 33 (9.09%)
occurrences (all)	1	13	4
RHINORRHOEA			
subjects affected / exposed	3 / 24 (12.50%)	1 / 37 (2.70%)	1 / 33 (3.03%)
occurrences (all)	4	1	1
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	6 / 24 (25.00%)	4 / 37 (10.81%)	1 / 33 (3.03%)
occurrences (all)	7	4	1
ATTENTION DEFICIT/HYPERACTIVITY DISORDER			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	1	2	1
DEPRESSION			

subjects affected / exposed	1 / 24 (4.17%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
ENURESIS			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
INSOMNIA			
subjects affected / exposed	1 / 24 (4.17%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	1	4	0
Investigations			
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	6 / 24 (25.00%)	3 / 37 (8.11%)	3 / 33 (9.09%)
occurrences (all)	7	3	7
CARNITINE DECREASED			
subjects affected / exposed	3 / 24 (12.50%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	3	0	2
ELECTROENCEPHALOGRAM ABNORMAL			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
INFLUENZA A VIRUS TEST POSITIVE			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
WEIGHT INCREASED			
subjects affected / exposed	0 / 24 (0.00%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
FALL			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	2	0	3
HAND FRACTURE			

subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	2	0	1
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	4	0
PROCEDURAL PAIN			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	1	2	2
STOMA SITE HYPERGRANULATION			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
Cardiac disorders			
CARDIOMYOPATHY			
subjects affected / exposed	3 / 24 (12.50%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	6	4	1
PALPITATIONS			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	5 / 24 (20.83%)	3 / 37 (8.11%)	5 / 33 (15.15%)
occurrences (all)	6	8	6
HYPOTONIA			
subjects affected / exposed	2 / 24 (8.33%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
LETHARGY			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
MIGRAINE			
subjects affected / exposed	1 / 24 (4.17%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	1 / 24 (4.17%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	2	0	1
MOTION SICKNESS			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	3 / 33 (9.09%)
occurrences (all)	0	0	3
Eye disorders			
ASTIGMATISM			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
HYPERMETROPIA			
subjects affected / exposed	1 / 24 (4.17%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
MYOPIA			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	3 / 24 (12.50%)	8 / 37 (21.62%)	6 / 33 (18.18%)
occurrences (all)	7	8	8
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 24 (0.00%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
ABDOMINAL PAIN			
subjects affected / exposed	2 / 24 (8.33%)	4 / 37 (10.81%)	8 / 33 (24.24%)
occurrences (all)	3	5	9
ABDOMINAL PAIN UPPER			
subjects affected / exposed	8 / 24 (33.33%)	7 / 37 (18.92%)	8 / 33 (24.24%)
occurrences (all)	17	18	16
CONSTIPATION			
subjects affected / exposed	3 / 24 (12.50%)	5 / 37 (13.51%)	5 / 33 (15.15%)
occurrences (all)	3	6	8
DENTAL CARIES			

subjects affected / exposed	2 / 24 (8.33%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	3	1	0
DIARRHOEA			
subjects affected / exposed	13 / 24 (54.17%)	15 / 37 (40.54%)	16 / 33 (48.48%)
occurrences (all)	19	30	29
DYSPEPSIA			
subjects affected / exposed	0 / 24 (0.00%)	3 / 37 (8.11%)	2 / 33 (6.06%)
occurrences (all)	0	3	2
GASTROINTESTINAL DISORDER			
subjects affected / exposed	3 / 24 (12.50%)	8 / 37 (21.62%)	5 / 33 (15.15%)
occurrences (all)	8	18	8
GASTROINTESTINAL PAIN			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	2	0	3
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 24 (4.17%)	4 / 37 (10.81%)	2 / 33 (6.06%)
occurrences (all)	2	4	2
NAUSEA			
subjects affected / exposed	7 / 24 (29.17%)	5 / 37 (13.51%)	6 / 33 (18.18%)
occurrences (all)	9	6	7
TOOTH IMPACTED			
subjects affected / exposed	0 / 24 (0.00%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
TOOTHACHE			
subjects affected / exposed	2 / 24 (8.33%)	1 / 37 (2.70%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
VOMITING			
subjects affected / exposed	13 / 24 (54.17%)	9 / 37 (24.32%)	13 / 33 (39.39%)
occurrences (all)	30	16	30
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	1 / 24 (4.17%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	1	4	1
DERMATITIS			

subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
DERMATITIS CONTACT			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	0	2	2
DERMATITIS DIAPER			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	4
RASH			
subjects affected / exposed	5 / 24 (20.83%)	3 / 37 (8.11%)	3 / 33 (9.09%)
occurrences (all)	6	3	4
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 24 (0.00%)	5 / 37 (13.51%)	0 / 33 (0.00%)
occurrences (all)	0	5	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 24 (8.33%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	2	5	0
BACK PAIN			
subjects affected / exposed	1 / 24 (4.17%)	3 / 37 (8.11%)	3 / 33 (9.09%)
occurrences (all)	1	3	4
MUSCLE SPASMS			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
MUSCULAR WEAKNESS			
subjects affected / exposed	3 / 24 (12.50%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	4	3	1
MYALGIA			
subjects affected / exposed	7 / 24 (29.17%)	8 / 37 (21.62%)	2 / 33 (6.06%)
occurrences (all)	16	30	2
PAIN IN EXTREMITY			
subjects affected / exposed	4 / 24 (16.67%)	3 / 37 (8.11%)	7 / 33 (21.21%)
occurrences (all)	11	5	20
RHABDOMYOLYSIS			

subjects affected / exposed	10 / 24 (41.67%)	18 / 37 (48.65%)	6 / 33 (18.18%)
occurrences (all)	22	81	8
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	1	2	1
CELLULITIS			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	3
CROUP INFECTIOUS			
subjects affected / exposed	1 / 24 (4.17%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
EAR INFECTION			
subjects affected / exposed	4 / 24 (16.67%)	2 / 37 (5.41%)	2 / 33 (6.06%)
occurrences (all)	5	2	2
GASTROENTERITIS			
subjects affected / exposed	4 / 24 (16.67%)	5 / 37 (13.51%)	2 / 33 (6.06%)
occurrences (all)	4	5	2
GASTROENTERITIS VIRAL			
subjects affected / exposed	4 / 24 (16.67%)	3 / 37 (8.11%)	2 / 33 (6.06%)
occurrences (all)	5	5	2
GASTROINTESTINAL VIRAL INFECTION			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	2	0	2
INFECTIOUS MONONUCLEOSIS			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
INFLUENZA			
subjects affected / exposed	3 / 24 (12.50%)	7 / 37 (18.92%)	4 / 33 (12.12%)
occurrences (all)	3	8	4
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
OTITIS EXTERNA			

subjects affected / exposed	2 / 24 (8.33%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	2	0	1
OTITIS MEDIA			
subjects affected / exposed	2 / 24 (8.33%)	3 / 37 (8.11%)	4 / 33 (12.12%)
occurrences (all)	3	5	7
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	0 / 37 (0.00%)	2 / 33 (6.06%)
occurrences (all)	0	0	2
PHARYNGITIS			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	0	1	2
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 24 (0.00%)	1 / 37 (2.70%)	7 / 33 (21.21%)
occurrences (all)	0	1	10
PNEUMONIA			
subjects affected / exposed	1 / 24 (4.17%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	2	1	3
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 24 (0.00%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
RHINITIS			
subjects affected / exposed	3 / 24 (12.50%)	0 / 37 (0.00%)	1 / 33 (3.03%)
occurrences (all)	5	0	1
SINUSITIS			
subjects affected / exposed	3 / 24 (12.50%)	5 / 37 (13.51%)	4 / 33 (12.12%)
occurrences (all)	4	9	5
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	13 / 24 (54.17%)	23 / 37 (62.16%)	11 / 33 (33.33%)
occurrences (all)	22	38	18
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 24 (4.17%)	7 / 37 (18.92%)	1 / 33 (3.03%)
occurrences (all)	2	11	1
VIRAL UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	6 / 24 (25.00%)	19 / 37 (51.35%)	8 / 33 (24.24%)
occurrences (all)	25	40	21
Metabolism and nutrition disorders			
ABNORMAL WEIGHT GAIN			
subjects affected / exposed	0 / 24 (0.00%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
DECREASED APPETITE			
subjects affected / exposed	1 / 24 (4.17%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	1	1	2
DEHYDRATION			
subjects affected / exposed	2 / 24 (8.33%)	4 / 37 (10.81%)	1 / 33 (3.03%)
occurrences (all)	2	8	1
FLUID OVERLOAD			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 24 (4.17%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	5	2	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
HYPOKALAEMIA			
subjects affected / exposed	1 / 24 (4.17%)	3 / 37 (8.11%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	3	0
HYPOPHAGIA			
subjects affected / exposed	0 / 24 (0.00%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
OBESITY			
subjects affected / exposed	0 / 24 (0.00%)	3 / 37 (8.11%)	1 / 33 (3.03%)
occurrences (all)	0	3	1

Non-serious adverse events	All Participants		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	90 / 94 (95.74%)		
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	7		
POOR VENOUS ACCESS			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	4		
FATIGUE			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	8		
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	6		
PAIN			
subjects affected / exposed	6 / 94 (6.38%)		
occurrences (all)	8		
PYREXIA			
subjects affected / exposed	19 / 94 (20.21%)		
occurrences (all)	35		
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
HYPERSENSITIVITY			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
SEASONAL ALLERGY			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			

ATELECTASIS			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
COUGH			
subjects affected / exposed	15 / 94 (15.96%)		
occurrences (all)	20		
DYSPNOEA			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	6		
HYPOXIA			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
NASAL CONGESTION			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	11		
OROPHARYNGEAL PAIN			
subjects affected / exposed	8 / 94 (8.51%)		
occurrences (all)	8		
RESPIRATORY DISORDER			
subjects affected / exposed	13 / 94 (13.83%)		
occurrences (all)	18		
RHINORRHOEA			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	6		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	11 / 94 (11.70%)		
occurrences (all)	12		
ATTENTION DEFICIT/HYPERACTIVITY DISORDER			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
DEPRESSION			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
ENURESIS			

subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
INSOMNIA			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	5		
Investigations			
BLOOD CHOLESTEROL INCREASED			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	12 / 94 (12.77%)		
occurrences (all)	17		
CARNITINE DECREASED			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	5		
ELECTROENCEPHALOGRAM ABNORMAL			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
INFLUENZA A VIRUS TEST POSITIVE			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
WEIGHT INCREASED			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
FALL			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	5		
HAND FRACTURE			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
LIGAMENT SPRAIN			

subjects affected / exposed occurrences (all) PROCEDURAL PAIN subjects affected / exposed occurrences (all) STOMA SITE HYPERGRANULATION subjects affected / exposed occurrences (all)	2 / 94 (2.13%) 4 4 / 94 (4.26%) 5 2 / 94 (2.13%) 2		
Cardiac disorders CARDIOMYOPATHY subjects affected / exposed occurrences (all) PALPITATIONS subjects affected / exposed occurrences (all)	 7 / 94 (7.45%) 11 2 / 94 (2.13%) 2		
Nervous system disorders HEADACHE subjects affected / exposed occurrences (all) HYPOTONIA subjects affected / exposed occurrences (all) LETHARGY subjects affected / exposed occurrences (all) MIGRAINE subjects affected / exposed occurrences (all) NEUROPATHY PERIPHERAL subjects affected / exposed occurrences (all)	 13 / 94 (13.83%) 20 3 / 94 (3.19%) 3 3 / 94 (3.19%) 3 4 / 94 (4.26%) 4 4 / 94 (4.26%) 4		
Blood and lymphatic system disorders ANAEMIA subjects affected / exposed occurrences (all)	 3 / 94 (3.19%) 3		
Ear and labyrinth disorders			

EAR PAIN			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
MOTION SICKNESS			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Eye disorders			
ASTIGMATISM			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
HYPERMETROPIA			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
MYOPIA			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	17 / 94 (18.09%)		
occurrences (all)	23		
ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
ABDOMINAL PAIN			
subjects affected / exposed	14 / 94 (14.89%)		
occurrences (all)	17		
ABDOMINAL PAIN UPPER			
subjects affected / exposed	23 / 94 (24.47%)		
occurrences (all)	51		
CONSTIPATION			
subjects affected / exposed	13 / 94 (13.83%)		
occurrences (all)	17		
DENTAL CARIES			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	4		
DIARRHOEA			

subjects affected / exposed	44 / 94 (46.81%)		
occurrences (all)	78		
DYSPEPSIA			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	5		
GASTROINTESTINAL DISORDER			
subjects affected / exposed	16 / 94 (17.02%)		
occurrences (all)	34		
GASTROINTESTINAL PAIN			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	5		
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	8		
NAUSEA			
subjects affected / exposed	18 / 94 (19.15%)		
occurrences (all)	22		
TOOTH IMPACTED			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
TOOTHACHE			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
VOMITING			
subjects affected / exposed	35 / 94 (37.23%)		
occurrences (all)	76		
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	6		
DERMATITIS			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
DERMATITIS CONTACT			

subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	4		
DERMATITIS DIAPER			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	5		
RASH			
subjects affected / exposed	11 / 94 (11.70%)		
occurrences (all)	13		
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	7		
BACK PAIN			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	8		
MUSCLE SPASMS			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
MUSCULAR WEAKNESS			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	8		
MYALGIA			
subjects affected / exposed	17 / 94 (18.09%)		
occurrences (all)	48		
PAIN IN EXTREMITY			
subjects affected / exposed	14 / 94 (14.89%)		
occurrences (all)	36		
RHABDOMYOLYSIS			
subjects affected / exposed	34 / 94 (36.17%)		
occurrences (all)	111		
Infections and infestations			

BRONCHITIS				
subjects affected / exposed	4 / 94 (4.26%)			
occurrences (all)	4			
CELLULITIS				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences (all)	3			
CROUP INFECTIOUS				
subjects affected / exposed	3 / 94 (3.19%)			
occurrences (all)	3			
EAR INFECTION				
subjects affected / exposed	8 / 94 (8.51%)			
occurrences (all)	9			
GASTROENTERITIS				
subjects affected / exposed	11 / 94 (11.70%)			
occurrences (all)	11			
GASTROENTERITIS VIRAL				
subjects affected / exposed	9 / 94 (9.57%)			
occurrences (all)	12			
GASTROINTESTINAL VIRAL INFECTION				
subjects affected / exposed	4 / 94 (4.26%)			
occurrences (all)	4			
INFECTIOUS MONONUCLEOSIS				
subjects affected / exposed	3 / 94 (3.19%)			
occurrences (all)	3			
INFLUENZA				
subjects affected / exposed	14 / 94 (14.89%)			
occurrences (all)	15			
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences (all)	2			
OTITIS EXTERNA				
subjects affected / exposed	3 / 94 (3.19%)			
occurrences (all)	3			
OTITIS MEDIA				

subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	15		
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
PHARYNGITIS			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	8 / 94 (8.51%)		
occurrences (all)	11		
PNEUMONIA			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	6		
POST PROCEDURAL INFECTION			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
RHINITIS			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	6		
SINUSITIS			
subjects affected / exposed	12 / 94 (12.77%)		
occurrences (all)	18		
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	47 / 94 (50.00%)		
occurrences (all)	78		
URINARY TRACT INFECTION			
subjects affected / exposed	9 / 94 (9.57%)		
occurrences (all)	14		
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	33 / 94 (35.11%)		
occurrences (all)	86		
Metabolism and nutrition disorders			

ABNORMAL WEIGHT GAIN			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
DECREASED APPETITE			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
DEHYDRATION			
subjects affected / exposed	7 / 94 (7.45%)		
occurrences (all)	11		
FLUID OVERLOAD			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
HYPERGLYCAEMIA			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	7		
HYPOCALCAEMIA			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
HYPOKALAEMIA			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	3		
HYPOPHAGIA			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
OBESITY			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 April 2015	• Inclusion criteria was revised to allow patients who have failed conventional therapy and who have documented severe unmet need and to provide additional detail on the acceptable methods of contraception. • Exclusion criteria was revised indicating that patients qualifying for any other clinical trial designed to progressively evaluate the safety and efficacy of UX007 in LC FAOD were not eligible. Criterion was also updated to exclude breastfeeding mothers from participation. • Stopping Rules were updated to state that Regulatory Authorities, Institutional Review Boards, and Ethics Committees will be informed should unexpected and possibly, probably, or definitely drug related serious adverse events (SAEs) occur and/or if the study is paused or stopped. Language was also added stating that, if paused or stopped, the trial will only be restarted following approval by Regulatory Authorities. • The PDMS and CGI scales were removed as efficacy variables. • Definitions for adverse event (AE) relatedness were updated. • Definitions for SAEs were clarified noting that hospitalizations planned prior to study enrollment (eg, elective surgeries) would not be considered SAEs and hospitalizations that occurred for pre-existing conditions that are scheduled after study enrollment are considered SAEs. • Sponsor's responsibilities with regard to reporting SAEs/suspected unexpected serious adverse reaction (SUSARs) were updated.
21 December 2015	• The term "Screening" was changed to "Baseline" • Deleted the sentence: "For subjects completing the UX007 CL201 study, the last evaluable echocardiogram will serve as Baseline for this study" • Added pancreatic lipase inhibitors and removed oral salicylates from the list of prohibited medications.
12 April 2016	• Clarified the total duration of the study indicating that patients will be treated with triheptanoin for up to 3 years or until market approval, whichever occurs first

16 September 2016	• Increased the length of a subject's study participation to up to 5 years (60 months; end of treatment visit) or until market approval, whichever occurred first. • Added that subjects who switched from medium chain triglyceride (MCT) to UX007 could transition at the same dose and then titrate, as appropriate. • Inclusion criteria was updated to define female subjects of child-bearing potential for whom pregnancy testing was required and subjects and their partners who must use contraception. • Examples of highly effective contraception methods were added. • The 12-Minute Walk Test and Pediatric Evaluation of Disability Inventory – Computer Adaptive Test were removed from the protocol • Added a Safety Follow-up Phone Call 30 to 35 days after the last dose of triheptanoin • Clarified that the End-of-study was the last subject's Safety Follow-up Phone Call • Clarified MCT oil and metabolic formulas containing significant contributions from MCT oil, including coconut oil, after the first dose of study medication were prohibited. • Updated the description of LC FAOD major events to state that if events occurred that represented a substantive change in the nature or an increase in frequency from a subject's prior medical history, the event was to be reported as an AE. • Removed the efficacy measures of subject-reported fatigue, exercise tolerance, muscle pain, and activity level efficacy recording from the protocol • Clarified that height, weight, and head circumference (if applicable) data would be evaluated using published normative data. • Increased the record retention period for all study records to at least 25 years after the end of the clinical trial or in accordance with national law. • Updated the description of the AE reporting process.
02 October 2017	• Added a pharmacokinetic (PK) substudy to characterize the steady-state PK of UX007 and UX007 metabolites in a subset of subjects (minimum of 12 subjects) at selected sites. Added PK analysis as a secondary objective and PK endpoints • Expanded UX007 dosing to allow doses greater than the upper level of the target range (25 to 35% of total daily caloric intake [DCI]) at the Investigator's discretion. This allowed subjects who enrolled from other studies on doses above the target range to continue on their current dose. • Modified the description of the physical examination to specify that the genitourinary component of the examination would be performed as age-appropriate at the Investigator's discretion based on clinical judgement and/or safety need. • Specified the primary, secondary, and exploratory endpoints in the synopsis and in the statistical methods section based on the study objectives and also specified that exploratory endpoints were to characterize the potential effect of UX007 treatment on functional disability and cognitive development, clinical biomarkers, and growth measurements. • Added text to clarify the SAE severity (Grade 3 or higher) to be considered by the Investigator for the study stopping rules.

01 October 2019	• Extended study duration from 5 years to up to 7 years or until commercial availability of UX007 in any region, whichever occurs first. An End of Study Visit was added in the case of commercial availability. • Increased the planned number of subjects from approximately 100 subjects to approximately 150 subjects. • Modified exclusion criterion #3 to allow exclusion of subjects who may be at increased risk of hypersensitivity adverse effects per the judgment of the Investigator. • Modified inclusion criterion #2 from "severe unmet need" to "clear unmet need" to more accurately reflect the clinical presentation of LC-FAOD in the study population. • Added clarifying language to allow for echocardiogram assessments performed as routine care within 30 days prior to the scheduled clinic visits. • Added clarifying language regarding the lymphatic portion of the physical examination to ensure that the exam scope is age appropriate and at the Investigator's discretion based on clinical judgement. • Added text to clarify the SAE severity (Grade 3 or higher) to be considered by the Investigator for the study stopping rules.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported