Clinical trial results:
A Phase III, Long Term, Open Label, Follow on Study of Microsomal Triglyceride Transfer Protein (MTP) Inhibitor 'lomitapide' (AEGR-733) in Patients with Homozygous Familial Hypercholesterolemia

Summary

EudraCT number	2010-023742-79
Trial protocol	IT
Global end of trial date	01 December 2014

Results information

Result version number	v1 (current)
This version publication date	26 April 2018
First version publication date	26 April 2018

Trial information

Trial identification

Sponsor protocol code	AEG 733-012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00943306
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aegerion Pharmaceuticals, Inc.
Sponsor organisation address	One Main Street, Suite 800, Cambridge, United States, 02142
Public contact	Agnieszka Jurecka, MD, PhD, Aegerion Pharmaceuticals, +1 857-242-5140, agnieszka.jurecka@aegerion.com
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 December 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy of lomitapide, as defined by percent change in LDL-C at the maximum tolerated dose at Week 48 compared to baseline, in combination with other lipid lowering therapy in patients with homozygous familial hypercholesterolemia (FH) who completed study UP1002 or 733-005.

Protection of trial subjects:

Although patients entered this study with a defined personal MTD of lomitapide (based on the MTD established during the first 26 weeks of treatment on Study UP1002/AEGR-733-005), a dose modification schedule was used if the patient required dose reduction in response to an AE or other factor

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2009
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	Italy: 5
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	South Africa: 9
Worldwide total number of subjects	19
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were eligible for inclusion in the study if they completed Study UP1002/AEGR-733-005 and were willing and able to provide consent and comply with local requirements of the study protocol.

Pre-assignment

Screening details:

Patients who met any of the stopping rules for study discontinuation at the final Study of UP 1002/AEGR-733-005 were excluded from the study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	All patients

Arm description:

Maximum tolerated dose of lomitapide in addition to existing lipid lowering therapy including plasmapheresis or lipid apheresis.

Arm type	Experimental
Investigational medicinal product name	Lomitapide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lomitapide mesylate capsules, 5 mg or 20 mg, were administered orally once per day. During Study UP1002/AEGR-733-005, the dose was initiated at 5 mg/day for 2 weeks and escalated at 4-week intervals (as tolerated) to 60 mg/day. Patients' specific doses for AEGR-733-012 were carried forward from UP1002/AEGR-733-005, but did not exceed the MTD that patients received during the original study.

Number of subjects in period 1	All patients
Started	19
Completed	16
Not completed	3
Adverse event, serious fatal	1
Physician decision	1
Sponsor decision due to non-compliance	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	19	19	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	19	19	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	30.4		
standard deviation	± 11.74	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	10	10	

End points

End points reporting groups

Reporting group title	All patients

Reporting group description:

Maximum tolerated dose of lomitapide in addition to existing lipid lowering therapy including plasmapheresis or lipid apheresis.

Subject analysis set title	Week 126 Completers Population
Subject analysis set type	Safety analysis

Subject analysis set description:

17 of 19 patients were included in the Week 126 Completers Population. One patient was terminated from treatment prior to Week 126 due to investigator decision. One patient continued treatment beyond Week 126 but did not have the visit conducted as scheduled (the patient temporarily discontinued from treatment due to a planned pregnancy; following delivery of a healthy baby, she returned to the study and completed treatment).

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population includes all patients who took at least one dose of study drug.

Primary: Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 126

End point title	Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 126[1]

End point description:

Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Primary

End point timeframe:

Baseline and Week 126

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics [arithmetic mean, arithmetic standard deviation, median, minimum (min), maximum (max), and number of subjects (N)] will be used to summarize results for the primary efficacy endpoint LDL-C

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-45.5 (± 31.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 174

End point title	Percent Change in Low Density Lipoprotein Cholesterol (LDL-C)

	- Week 174

End point description:

Percent change in Low Density Lipoprotein Cholesterol (LDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	-51.0 (± 16.03)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 222

End point title	Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 222

End point description:

Percent change in Low Density Lipoprotein Cholesterol (LDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-58.5 (± 24.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 246

End point title	Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 246

End point description:

Percent change in Low Density Lipoprotein Cholesterol (LDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-60.1 (± 18.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 270

End point title	Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 270

End point description:

Percent change in Low Density Lipoprotein Cholesterol (LDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-74.0 (± 19.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 294

End point title	Percent Change in Low Density Lipoprotein Cholesterol (LDL-C) - Week 294

End point description:

Percent change in Low Density Lipoprotein Cholesterol (LDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-51.1 (± 10.11)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Cholesterol - Week 126

End point title	Percent Change in Total Cholesterol - Week 126

End point description:

Percent change in Total Cholesterol from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-43.2 (± 25.35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Cholesterol - Week 174

End point title	Percent Change in Total Cholesterol - Week 174

End point description:

Percent change in Total Cholesterol from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	-46.9 (± 15.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Cholesterol - Week 222

End point title	Percent Change in Total Cholesterol - Week 222

End point description:

Percent change in Total Cholesterol from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-51.0 (± 21.34)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Cholesterol - Week 246

End point title	Percent Change in Total Cholesterol - Week 246

End point description:

Percent change in Total Cholesterol from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-54.1 (± 16.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Cholesterol - Week 270

End point title	Percent Change in Total Cholesterol - Week 270

End point description:

Percent change in Total Cholesterol from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-65.2 (± 15.97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Cholesterol - Week 294

End point title	Percent Change in Total Cholesterol - Week 294

End point description:

Percent change in Total Cholesterol from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-43.9 (± 5.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein B (Apo B) - Week 126

End point title	Percent Change in Apolipoprotein B (Apo B) - Week 126

End point description:

Percent change in Apolipoprotein B (Apo B) from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-53.6 (± 23.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein B (Apo B) - Week 174

End point title	Percent Change in Apolipoprotein B (Apo B) - Week 174

End point description:

Percent change in Apolipoprotein B (Apo B) from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	-59.4 (± 12.60)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein B (Apo B) - Week 222

End point title	Percent Change in Apolipoprotein B (Apo B) - Week 222

End point description:

Percent change in Apolipoprotein B (Apo B) from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-65.1 (± 20.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein B (Apo B) - Week 246

End point title	Percent Change in Apolipoprotein B (Apo B) - Week 246

End point description:

Percent change in Apolipoprotein B (Apo B) from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-65.9 (± 15.76)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein B (Apo B) - Week 270

End point title	Percent Change in Apolipoprotein B (Apo B) - Week 270

End point description:

Percent change in Apolipoprotein B (Apo B) from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-76.7 (± 16.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein B (Apo B) - Week 294

End point title	Percent Change in Apolipoprotein B (Apo B) - Week 294

End point description:

Percent change in Apolipoprotein B (Apo B) from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-60.9 (± 12.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Triglycerides - Week 126

End point title	Percent Change in Triglycerides - Week 126

End point description:

Percent change in Triglycerides from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-37.5 (± 42.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Triglycerides - Week 174

End point title	Percent Change in Triglycerides - Week 174

End point description:

Percent change in Triglycerides from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	-31.7 (± 37.09)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Triglycerides - Week 222

End point title	Percent Change in Triglycerides - Week 222

End point description:

Percent change in Triglycerides from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-27.6 (± 48.88)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Triglycerides - Week 246

End point title	Percent Change in Triglycerides - Week 246

End point description:

Percent change in Triglycerides from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-41.9 (± 33.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Triglycerides - Week 270

End point title	Percent Change in Triglycerides - Week 270

End point description:

Percent change in Triglycerides from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-48.5 (± 34.24)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Triglycerides - Week 294

End point title	Percent Change in Triglycerides - Week 294

End point description:

Percent change in Triglycerides from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	29.2 (± 58.74)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 126

End point title	Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 126

End point description:

Percent change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-47.1 (± 27.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 174

End point title	Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 174

End point description:

Percent change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	-53.5 (± 16.42)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 222

End point title	Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 222

End point description:

Percent change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-57.0 (± 24.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 246

End point title	Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 246

End point description:

Percent change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-58.8 (± 17.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 270

End point title	Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 270

End point description:

Percent change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-71.5 (± 17.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 294

End point title	Percent Change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) - Week 294

End point description:

Percent change in Non High Density Lipoprotein Cholesterol (Non-HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-46.6 (± 5.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 126

End point title	Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 126

End point description:

Percent change in Very Low Density Lipoprotein Cholesterol (VLDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-36.8 (± 43.90)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 174

End point title	Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 174

End point description:

Percent change in Very Low Density Lipoprotein Cholesterol (VLDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	-31.5 (± 36.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 222

End point title	Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 222

End point description:	
Percent change in Very Low Density Lipoprotein Cholesterol (VLDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).	
End point type	Secondary
End point timeframe:	
Baseline and Week 222	

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-26.3 (± 49.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 246

End point title	Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 246
End point description:	
Percent change in Very Low Density Lipoprotein Cholesterol (VLDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).	
End point type	Secondary
End point timeframe:	
Baseline and Week 246	

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-41.4 (± 34.20)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 270

End point title	Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 270

End point description:

Percent change in Very Low Density Lipoprotein Cholesterol (VLDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-48.7 (± 33.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 294

End point title	Percent Change in Very Low Density Lipoprotein Cholesterol (VLDL-C) - Week 294

End point description:

Percent change in Very Low Density Lipoprotein Cholesterol (VLDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-30.6 (± 59.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Lp(a) - Week 126

End point title	Percent Change in Lp(a) - Week 126

End point description:

Percent change in Lp(a) from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	5.5 (± 43.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Lp(a) - Week 174

End point title	Percent Change in Lp(a) - Week 174

End point description:

Percent change in Lp(a) from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	10.2 (± 60.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Lp(a) - Week 222

End point title	Percent Change in Lp(a) - Week 222

End point description:

Percent change in Lp(a) from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-12.8 (± 49.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Lp(a) - Week 246

End point title	Percent Change in Lp(a) - Week 246

End point description:

Percent change in Lp(a) from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: percent change				
arithmetic mean (standard deviation)	3.4 (± 54.22)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Lp(a) - Week 270

End point title	Percent Change in Lp(a) - Week 270

End point description:

Percent change in Lp(a) from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-6.6 (± 48.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Lp(a) - Week 294

End point title	Percent Change in Lp(a) - Week 294

End point description:

Percent change in Lp(a) from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-10.4 (± 35.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 126

End point title	Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 126

End point description:

Percent change in High Density Lipoprotein Cholesterol (HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-8.3 (± 19.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 174

End point title	Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 174

End point description:

Percent change in High Density Lipoprotein Cholesterol (HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	3.8 (± 26.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 222

End point title	Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 222

End point description:

Percent change in High Density Lipoprotein Cholesterol (HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-2.7 (± 21.22)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 246

End point title	Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 246

End point description:

Percent change in High Density Lipoprotein Cholesterol (HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: percent change				
arithmetic mean (standard deviation)	-12.5 (± 19.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 270

End point title	Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 270

End point description:

Percent change in High Density Lipoprotein Cholesterol (HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-10.3 (± 27.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 294

End point title	Percent Change in High Density Lipoprotein Cholesterol (HDL-C) - Week 294

End point description:

Percent change in High Density Lipoprotein Cholesterol (HDL-C) from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-23.5 (± 2.27)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein AI (Apo AI) - Week 126

End point title	Percent Change in Apolipoprotein AI (Apo AI) - Week 126

End point description:

Percent change in Apolipoprotein AI (Apo AI) from Baseline (Week 0 of Study 733-005/UP1002) and Week 126 (Week 48 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 126

End point values	Week 126 Completers Population			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: percent change				
arithmetic mean (standard deviation)	-14.0 (± 17.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein AI (Apo AI) - Week 174

End point title	Percent Change in Apolipoprotein AI (Apo AI) - Week 174

End point description:

Percent change in Apolipoprotein AI (Apo AI) from Baseline (Week 0 of Study 733-005/UP1002) and Week 174 (Week 96 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 174

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	16			
Units: percent change				
arithmetic mean (standard deviation)	-8.2 (± 20.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein AI (Apo AI) - Week 222

End point title	Percent Change in Apolipoprotein AI (Apo AI) - Week 222

End point description:

Percent change in Apolipoprotein AI (Apo AI) from Baseline (Week 0 of Study 733-005/UP1002) and Week 222 (Week 144 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 222

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-2.7 (± 33.30)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein AI (Apo AI) - Week 246

End point title	Percent Change in Apolipoprotein AI (Apo AI) - Week 246

End point description:

Percent change in Apolipoprotein AI (Apo AI) from Baseline (Week 0 of Study 733-005/UP1002) and Week 246 (Week 168 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 246

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: percent change				
arithmetic mean (standard deviation)	-16.8 (± 26.62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein AI (Apo AI) - Week 270

End point title	Percent Change in Apolipoprotein AI (Apo AI) - Week 270

End point description:

Percent change in Apolipoprotein AI (Apo AI) from Baseline (Week 0 of Study 733-005/UP1002) and Week 270 (Week 192 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 270

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: percent change				
arithmetic mean (standard deviation)	-17.8 (± 20.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Apolipoprotein AI (Apo AI) - Week 294

End point title	Percent Change in Apolipoprotein AI (Apo AI) - Week 294

End point description:

Percent change in Apolipoprotein AI (Apo AI) from Baseline (Week 0 of Study 733-005/UP1002) and Week 294 (Week 216 in Study AEGR-733-012).

End point type	Secondary

End point timeframe:

Baseline and Week 294

End point values	Safety Population			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: percent change				
arithmetic mean (standard deviation)	-30.5 (± 22.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Week 78 of Study 733-005/UP1002 to Week 294 of Study 733-005/UP1002 (Week 216 of Study AEGR-733-012)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups	
Reporting group title	All patients
Reporting group description:	
Maximum tolerated dose of lomitapide in addition to existing lipid lowering therapy including plasmapheresis or lipid apheresis.	

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 19 (36.84%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Investigations			
International normalised ratio increased			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteriovenous fistula			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypovolaemic shock			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aortic valve incompetence			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Anticoagulant therapy			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transfusion			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Facial palsy			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Sudden cardiac death			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reflux oesophagitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 19 (89.47%)		
Vascular disorders			
Arterial stenosis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Arteriovenous fistula			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hypovolaemic shock			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Surgical and medical procedures			
Anticoagulant therapy			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Transfusion			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

Fatigue subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Sudden cardiac death subjects affected / exposed occurrences (all) Vestibulitis subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 2 / 19 (10.53%) 2 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1 1 / 19 (5.26%) 1		
Immune system disorders Drug hypersensitivity subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 3		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Respiratory, thoracic and mediastinal disorders Apnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1 2 / 19 (10.53%) 2		

Dyspnoea			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Dyspnoea exertional			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Painful respiration			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Pharyngolaryngeal pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Sinus congestion			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	4		
Depression			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	6		
Stress			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	7		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	4		
Blood potassium increased			

subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood pressure increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Blood creatine phosphokinase increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Carotid bruit				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	5			
International normalised ratio decreased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
International normalised ratio increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	2			
Liver function test abnormal				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	2			
Prothrombin time prolonged				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Transaminases increased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	5			
Vitamin K decreased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Weight decreased				
subjects affected / exposed	2 / 19 (10.53%)			
occurrences (all)	2			
White blood cell count decreased				

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Joint injury			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	3		
Post procedural diarrhoea			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Procedural headache			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Skeletal injury			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Subdural haematoma			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	12		
Aortic valve incompetence			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Chest pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Coronary artery disease			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Sinus bradycardia			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	4		
Facial Palsy			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	6 / 19 (31.58%)		
occurrences (all)	10		
Hypoaesthesia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Migraine			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Paraesthesia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	8		
Sensory disturbance			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Iron deficiency anaemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	3		
Ear and labyrinth disorders			

Tinnitus			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	4		
Chapped lips			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	8 / 19 (42.11%)		
occurrences (all)	25		
Dyspepsia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Epigastric discomfort			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	4		
Flatulence			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	4		
Gingival bleeding			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Hiatus hernia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Intestinal mass			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	6 / 19 (31.58%)		
occurrences (all)	17		
Reflux oesophagitis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
stomach discomfort			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	5 / 19 (26.32%)		
occurrences (all)	9		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Dry skin			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Hair growth abnormal			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Scar			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Rhabdomyolysis			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Tendonitis			
subjects affected / exposed	2 / 19 (10.53%)		
occurrences (all)	2		
Infections and infestations			

Bronchitis				
subjects affected / exposed	3 / 19 (15.79%)			
occurrences (all)	4			
Gastroenteritis				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	4			
Gastrointestinal infection				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	5 / 19 (26.32%)			
occurrences (all)	8			
Lower respiratory tract infection				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	4 / 19 (21.05%)			
occurrences (all)	11			
Sinusitis				
subjects affected / exposed	3 / 19 (15.79%)			
occurrences (all)	3			
Tooth abscess				
subjects affected / exposed	2 / 19 (10.53%)			
occurrences (all)	2			
Upper respiratory tract infection				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	2			
Urinary tract infection				
subjects affected / exposed	2 / 19 (10.53%)			
occurrences (all)	2			
Viral infection				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			
Carotene decreased				
subjects affected / exposed	1 / 19 (5.26%)			
occurrences (all)	1			

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Dehydration			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	4		
Oral intake reduced			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	2		
Vitamin E deficiency			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported