Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of Varying Doses and Dose Regimens of Evinacumab in Patients with Persistent Hypercholesterolemia Despite Maximally Tolerated Lipid Modifying Therapy

Summary

EudraCT number	2017-001508-31
Trial protocol	CZ NL NO SE DK PL AT ES GB
Global end of trial date	14 December 2020

Results information

Result version number	v1 (current)
This version publication date	29 December 2021
First version publication date	29 December 2021

Trial information

Trial identification

Sponsor protocol code	R1500-CL-1643

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03175367
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, United States, 10591
Public contact	Clinical Trial Adminstrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trial Adminstrator, Regeneron Pharmaceuticals, Inc., 001 8447346643, clinicaltrials@regeneron.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	14 December 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 December 2020
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 reduction of LDL-C by evinacumab in comparison to placebo after 16 weeks in subjects with primary hypercholesterolemia (HeFH, or non-HeFH with a history of clinical ASCVD) with persistent hypercholesterolemia despite receiving maximally-tolerated LMT. Persistent hypercholesterolemia is defined as LDL-C ≥70 mg/dL (1.81 mmol/L) for those subjects with clinical ASCVD and LDL-C ≥100 mg/dL (2.59 mmol/L) for those subjects without clinical ASCVD.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Council for Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	Jordan: 19
Country: Number of subjects enrolled	Netherlands: 21
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Norway: 7
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Russian Federation: 31
Country: Number of subjects enrolled	South Africa: 23
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	Sweden: 5

Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 75
Worldwide total number of subjects	266
EEA total number of subjects	86

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)	214
From 65 to 84 years	52
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study participants were recruited from 20 countries in Europe, Africa, Asia, North America, and Australasia

Pre-assignment

Screening details:

A total of 327 participants were screened and 272 participants randomized. 6 participants were randomized but never treated.

Period 1

Period 1 title	Double-blind treatment period (DBTP)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A: Placebo SC QW (DBTP)

Arm description:

Placebo Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo of Evinacumab subcutaneous treatment

Arm title	Group A: Evinacumab 300mg SC Q2W (DBTP)

Arm description:

Evinacumab 300 mg Subcutaneous (SC) treatment every other week (alternating with placebo on opposite weeks) for 16 weeks followed by a 23-week follow-up period

Arm type	Experimental
Investigational medicinal product name	Evinacumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Evinacumab subcutaneous treatment

Arm title	Group A: Evinacumab 300mg SC QW (DBTP)

Arm description:

Evinacumab 300 mg Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period

Arm type	Experimental

Investigational medicinal product name	Evinacumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Evinacumab subcutaneous treatment

Arm title	Group A: Evinacumab 450mg SC QW (DBTP)

Arm description:

Evinacumab 450 mg Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period.

Arm type	Experimental
Investigational medicinal product name	Evinacumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Evinacumab subcutaneous treatment

Arm title	Group B: Placebo IV Q4W (DBTP)

Arm description:

Placebo Intravenous (IV) treatment every 4 weeks for 24 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo of Evinacumab intravenous treatment

Arm title	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)

Arm description:

Evinacumab 5mg/kg IV treatment every 4 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.

Arm type	Experimental
Investigational medicinal product name	Evinacumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Evinacumab intravenous treatment

Arm title	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)

Arm description:

Evinacumab 5mg/kg IV treatment every 4 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.

Arm type	Experimental

Investigational medicinal product name	Evinacumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Evinacumab intravenous treatment

Number of subjects in period 1	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)
Started	39	39	42
Completed	30	31	30
Not completed	9	8	12
Consent withdrawn by subject	1	1	2
Physician decision	6	5	8
Adverse event, non-fatal	2	2	-
Lost to follow-up	-	-	1
Protocol deviation	-	-	1

Number of subjects in period 1	Group A: Evinacumab 450mg SC QW (DBTP)	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Started	40	33	35
Completed	30	31	32
Not completed	10	2	3
Consent withdrawn by subject	2	-	1
Physician decision	6	-	-
Adverse event, non-fatal	-	1	2
Lost to follow-up	-	1	-
Protocol deviation	2	-	-

Number of subjects in period 1	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Started	38
Completed	34
Not completed	4
Consent withdrawn by subject	-
Physician decision	-
Adverse event, non-fatal	2
Lost to follow-up	-
Protocol deviation	2

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group B: DB Placebo IV Q4W (OLTP)

Arm description:

Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.

Arm type	Experimental
Investigational medicinal product name	Evinacumab intravenous treatment
Investigational medicinal product code	Evinacumab
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Evinacumab intravenous treatment

Arm title	Group B: DB Evinacumab 5mg/kg IV Q4W (OLTP)

Arm description:

Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.

Arm type	Experimental
Investigational medicinal product name	Evinacumab intravenous treatment
Investigational medicinal product code	Evinacumab
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Evinacumab intravenous treatment

Arm title	Group B: DB Evinacumab 15mg/kg IV Q4W (OLTP)

Arm description:

Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.

Arm type	Experimental
Investigational medicinal product name	Evinacumab intravenous treatment
Investigational medicinal product code	Evinacumab
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Evinacumab intravenous treatment

Number of subjects in period 2[1]	Group B: DB Placebo IV Q4W (OLTP)	Group B: DB Evinacumab 5mg/kg IV Q4W (OLTP)	Group B: DB Evinacumab 15mg/kg IV Q4W (OLTP)
Started	31	32	34
Treated in OLTP	31	32	33
Completed	31	30	32
Not completed	0	2	2
Consent withdrawn by subject	-	2	1
Completed DBTP but did not continue to OLTP	-	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: All patients who successfully complete this study (or successfully complete the double-blind treatment period and open-label treatment period for patients in the IV treatment groups) may have the opportunity to enroll in an open-label extension or safety study. All patients who enroll in the open-label extension or safety study will continue to receive evinacumab.

Baseline characteristics

Reporting groups	
Reporting group title	Group A: Placebo SC QW (DBTP)
Reporting group description:	
Placebo Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period	
Reporting group title	Group A: Evinacumab 300mg SC Q2W (DBTP)
Reporting group description:	
Evinacumab 300 mg Subcutaneous (SC) treatment every other week (alternating with placebo on opposite weeks) for 16 weeks followed by a 23-week follow-up period	
Reporting group title	Group A: Evinacumab 300mg SC QW (DBTP)
Reporting group description:	
Evinacumab 300 mg Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period	
Reporting group title	Group A: Evinacumab 450mg SC QW (DBTP)
Reporting group description:	
Evinacumab 450 mg Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period.	
Reporting group title	Group B: Placebo IV Q4W (DBTP)
Reporting group description:	
Placebo Intravenous (IV) treatment every 4 weeks for 24 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	
Reporting group title	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Reporting group description:	
Evinacumab 5mg/kg IV treatment every 4 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	
Reporting group title	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Reporting group description:	
Evinacumab 5mg/kg IV treatment every 4 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	

Reporting group values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects	39	39	42
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	34	29	34
From 65-84 years	5	10	8
85 years and over	0	0	0

Age Continuous Units: years			
arithmetic mean	52.4	55.0	54.0
standard deviation	± 12.69	± 13.01	± 12.22
Sex: Female, Male Units:			
Female	27	21	23
Male	12	18	19
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	2	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	0	0
White	34	34	39
More than one race	0	0	0
Unknown or Not Reported	1	3	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	5	2
Not Hispanic or Latino	36	31	38
Unknown or Not Reported	1	3	2

Reporting group values	Group A: Evinacumab 450mg SC QW (DBTP)	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects	40	33	35
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	30	26	28
From 65-84 years	10	7	7
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	54.5	56.2	55.7
standard deviation	± 15.14	± 10.91	± 9.58
Sex: Female, Male Units:			
Female	29	18	22
Male	11	15	13
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	1

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	0
White	38	27	32
More than one race	0	0	0
Unknown or Not Reported	1	3	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	3	7
Not Hispanic or Latino	38	30	28
Unknown or Not Reported	0	0	0

Reporting group values	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	Total	
Number of subjects	38	266	
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)	33	214	
From 65-84 years	5	52	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	52.1		
standard deviation	± 12.12	-	
Sex: Female, Male			
Units:			
Female	19	159	
Male	19	107	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	5	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	6	
White	35	239	
More than one race	0	0	
Unknown or Not Reported	3	16	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	2	23	
Not Hispanic or Latino	36	237	
Unknown or Not Reported	0	6	

End points

End points reporting groups

Reporting group title	Group A: Placebo SC QW (DBTP)
Reporting group description:	
Placebo Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period	
Reporting group title	Group A: Evinacumab 300mg SC Q2W (DBTP)
Reporting group description:	
Evinacumab 300 mg Subcutaneous (SC) treatment every other week (alternating with placebo on opposite weeks) for 16 weeks followed by a 23-week follow-up period	
Reporting group title	Group A: Evinacumab 300mg SC QW (DBTP)
Reporting group description:	
Evinacumab 300 mg Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period	
Reporting group title	Group A: Evinacumab 450mg SC QW (DBTP)
Reporting group description:	
Evinacumab 450 mg Subcutaneous (SC) treatment every week for 16 weeks followed by a 23-week follow-up period.	
Reporting group title	Group B: Placebo IV Q4W (DBTP)
Reporting group description:	
Placebo Intravenous (IV) treatment every 4 weeks for 24 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	
Reporting group title	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Reporting group description:	
Evinacumab 5mg/kg IV treatment every 4 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	
Reporting group title	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Reporting group description:	
Evinacumab 5mg/kg IV treatment every 4 weeks. Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	
Reporting group title	Group B: DB Placebo IV Q4W (OLTP)
Reporting group description:	
Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	
Reporting group title	Group B: DB Evinacumab 5mg/kg IV Q4W (OLTP)
Reporting group description:	
Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	
Reporting group title	Group B: DB Evinacumab 15mg/kg IV Q4W (OLTP)
Reporting group description:	
Group B (IV treatment groups) entered a 48-week OLTP after completing the 24-week double-blind treatment period (DBTP) and received evinacumab 15 mg/kg IV Q4W regardless of their treatment assignment in the DBTP.	

Primary: Percent Change from Baseline in Calculated Low Density Lipoprotein Cholesterol (LDL-C) at Week 16 (ITT Estimand)

End point title	Percent Change from Baseline in Calculated Low Density Lipoprotein Cholesterol (LDL-C) at Week 16 (ITT Estimand)
End point description:	
End point type	Primary
End point timeframe: Week 16	

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percent Change				
least squares mean (standard error)	8.8 (± 6.4)	-29.7 (± 6.4)	-44.0 (± 6.3)	-47.2 (± 6.2)

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	0.6 (± 6.6)	-23.5 (± 6.6)	-49.9 (± 6.1)	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-38.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.5
upper limit	-20.6

Variability estimate	Standard error of the mean
Dispersion value	9.1

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-52.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-70.7
upper limit	-35.1
Variability estimate	Standard error of the mean
Dispersion value	9

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-73.7
upper limit	-38.3
Variability estimate	Standard error of the mean
Dispersion value	9

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0109 [1]
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-24.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.6
upper limit	-5.7
Variability estimate	Standard error of the mean
Dispersion value	9.3

Notes:

[1] - P-Value is not adjusted for multiplicity

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-50.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.4
upper limit	-32.6
Variability estimate	Standard error of the mean
Dispersion value	9

Secondary: Percent Change from Baseline in Apolipoprotein B (Apo B) at Week 16 (ITT Estimand)

End point title	Percent Change from Baseline in Apolipoprotein B (Apo B) at Week 16 (ITT Estimand)

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percent Change				
least squares mean (standard error)	6.7 (± 5.1)	-19.9 (± 5.1)	-35.2 (± 5.1)	-38.8 (± 4.9)

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	-3.8 (± 4.7)	-20.4 (± 4.6)	-43.2 (± 4.3)	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0003
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-26.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.9
upper limit	-12.4
Variability estimate	Standard error of the mean
Dispersion value	7.2

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)

Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.1
upper limit	-27.9
Variability estimate	Standard error of the mean
Dispersion value	7.1

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-45.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.5
upper limit	-31.5
Variability estimate	Standard error of the mean
Dispersion value	7.1

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0132
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-16.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.7
upper limit	-3.5
Variability estimate	Standard error of the mean
Dispersion value	6.6

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-39.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52
upper limit	-26.8
Variability estimate	Standard error of the mean
Dispersion value	6.4

Secondary: Percent Change from Baseline in Apo B at Week 24 (ITT Estimand)

End point title	Percent Change from Baseline in Apo B at Week 24 (ITT Estimand)[2]

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to those patients receiving IV route of study treatment administration

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	5.9 (± 6.0)	-15.9 (± 5.9)	-34.5 (± 5.6)	

Statistical analyses

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0111
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-21.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.4
upper limit	-5.1
Variability estimate	Standard error of the mean
Dispersion value	8.4

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-40.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-56.7
upper limit	-24
Variability estimate	Standard error of the mean
Dispersion value	8.2

Secondary: Percent Change from Baseline in Non High Density Lipoprotein Cholesterol (non-HDL-C) at Week 16 (ITT Estimand)

End point title	Percent Change from Baseline in Non High Density Lipoprotein

	Cholesterol (non-HDL-C) at Week 16 (ITT Estimand)

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 16

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percent Change				
least squares mean (standard error)	8.0 (± 5.4)	-31.3 (± 5.4)	-45.8 (± 5.3)	-50.6 (± 5.2)

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	-1.1 (± 5.8)	-24.8 (± 5.7)	-52.0 (± 5.3)	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-39.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.4
upper limit	-24.3
Variability estimate	Standard error of the mean
Dispersion value	7.6

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-53.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.8
upper limit	-38.9
Variability estimate	Standard error of the mean
Dispersion value	7.6

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-58.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-73.4
upper limit	-43.7
Variability estimate	Standard error of the mean
Dispersion value	7.5

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0042
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-23.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.7
upper limit	-7.7
Variability estimate	Standard error of the mean
Dispersion value	8.1

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-50.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.4
upper limit	-35.4
Variability estimate	Standard error of the mean
Dispersion value	7.8

Secondary: Percent Change from Baseline in non-HDL-C at Week 24 (ITT Estimand)

End point title	Percent Change from Baseline in non-HDL-C at Week 24 (ITT Estimand)[3]

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[3] - 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: This endpoint is only applicable to those patients receiving IV route of study treatment administration

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	10.4 (± 7.0)	-20.2 (± 6.7)	-44.3 (± 6.4)	

Statistical analyses

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0021
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-30.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.8
upper limit	-11.4
Variability estimate	Standard error of the mean
Dispersion value	9.7

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-54.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-73.4
upper limit	-35.8
Variability estimate	Standard error of the mean
Dispersion value	9.5

Secondary: Percentage of Participants with >= 30% Reduction in Calculated LDL-C at Week 16 (ITT Estimand)

End point title	Percentage of Participants with >= 30% Reduction in Calculated LDL-C at Week 16 (ITT Estimand)

End point description:

End point type	Secondary

End point timeframe:

Week 16

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percentage of Participants				
number (not applicable)	11.3	68.1	73.9	71.4

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percentage of Participants				
number (not applicable)	15.5	57.9	86.8	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	19.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	5.1
upper limit	72.8

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	23.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.4
upper limit	89.2

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	22.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	80.5

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0007
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	29.2

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Log odds ratio
Point estimate	42.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.4
upper limit	172.3

Secondary: Percentage of Participants with >= 50% Reduction in Calculated LDL-C at Week 16 (ITT Estimand)

End point title	Percentage of Participants with >= 50% Reduction in Calculated LDL-C at Week 16 (ITT Estimand)

End point description:

End point type	Secondary

End point timeframe:

Week 16

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percentage of Participants				
number (not applicable)	5.2	28.6	53.7	60.6

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percentage of Participants				
number (not applicable)	12.3	24.6	63.2	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	53.5

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	24.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.7
upper limit	129.9

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	36.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.7
upper limit	194.7

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3185
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	8.2

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	14.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	54.2

Secondary: Percentage of Participants with Calculated LDL-C < 50 mg/dL (1.30 mmol/L) at Week 16 (ITT Estimand)

End point title	Percentage of Participants with Calculated LDL-C < 50 mg/dL (1.30 mmol/L) at Week 16 (ITT Estimand)

End point description:

Percentage of Participants with Calculated LDL-C < 50 milligrams/deciliter (mg/dL) [1.30 Millimoles per liter (mmol/L)] at Week 16 (ITT Estimand)

End point type	Secondary

End point timeframe:

Week 16

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percentage of Participants				
number (not applicable)	5.1	22.8	29.7	40.8

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percentage of Participants				
number (not applicable)	9.3	13.2	39.5	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0718
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	26.5

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0048
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.1
upper limit	62.1

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0015
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	14.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	76.8

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.527
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	8.4

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0047
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	31.7

Secondary: Percent Change from Baseline in Calculated LDL-C at Week 24 (ITT Estimand)

End point title	Percent Change from Baseline in Calculated LDL-C at Week 24 (ITT Estimand)[4]
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and Week 24	

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to those patients receiving IV route of study treatment administration

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	14.8 (± 8.3)	-17.7 (± 8.0)	-39.7 (± 7.7)	

Statistical analyses

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0059
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-32.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.5
upper limit	-9.6
Variability estimate	Standard error of the mean
Dispersion value	11.5

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-54.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-77
upper limit	-32
Variability estimate	Standard error of the mean
Dispersion value	11.3

Secondary: Percent Change from Baseline in Total Cholesterol (TC) at Week 16 (ITT Estimand)

End point title	Percent Change from Baseline in Total Cholesterol (TC) at Week 16 (ITT Estimand)
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and Week 16	

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percent Change				
least squares mean (standard error)	6.1 (± 4.0)	-31.0 (± 4.0)	-40.3 (± 4.0)	-45.4 (± 3.9)

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	-0.4 (± 4.5)	-22.6 (± 4.4)	-46.8 (± 4.1)	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-37.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-48.4
upper limit	-25.8
Variability estimate	Standard error of the mean
Dispersion value	5.7

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-46.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.5
upper limit	-35.2
Variability estimate	Standard error of the mean
Dispersion value	5.6

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-51.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.5
upper limit	-40.4
Variability estimate	Standard error of the mean
Dispersion value	5.6

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-22.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.6
upper limit	-9.8
Variability estimate	Standard error of the mean
Dispersion value	6.2

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-46.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.4
upper limit	-34.4
Variability estimate	Standard error of the mean
Dispersion value	6.1

Secondary: Percent Change from Baseline in Total Cholesterol at Week 24 (ITT Estimand)

End point title	Percent Change from Baseline in Total Cholesterol at Week 24 (ITT Estimand)[5]

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[5] - 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: This endpoint is only applicable to those patients receiving IV route of study treatment administration

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	8.5 (± 5.1)	-19.9 (± 4.9)	-40.8 (± 4.7)	

Statistical analyses

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-28.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.6
upper limit	-14.3
Variability estimate	Standard error of the mean
Dispersion value	7.1

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-49.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.2
upper limit	-35.4
Variability estimate	Standard error of the mean
Dispersion value	7

Secondary: Percent Change from Baseline in Fasting Triglycerides at Week 16 (ITT Estimand)

End point title	Percent Change from Baseline in Fasting Triglycerides at Week 16 (ITT Estimand)
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and Week 16	

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percent Change				
least squares mean (standard error)	8.1 (± 4.5)	-38.0 (± 4.2)	-47.7 (± 4.0)	-53.4 (± 3.9)

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	-6.9 (± 4.7)	-32.1 (± 4.5)	-52.8 (± 4.1)	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-46.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.8
upper limit	-34.3
Variability estimate	Standard error of the mean
Dispersion value	6

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-55.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-67.3
upper limit	-44.3
Variability estimate	Standard error of the mean
Dispersion value	5.9

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-61.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-72.9
upper limit	-50
Variability estimate	Standard error of the mean
Dispersion value	5.8

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-25.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38
upper limit	-12.4
Variability estimate	Standard error of the mean
Dispersion value	6.5

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-45.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.4
upper limit	-33.5
Variability estimate	Standard error of the mean
Dispersion value	6.3

Secondary: Percent Change from Baseline in Fasting Triglycerides at Week 24 (ITT Estimand)

End point title	Percent Change from Baseline in Fasting Triglycerides at Week 24 (ITT Estimand)[6]

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only applicable to those patients receiving IV route of study treatment administration

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	-6.1 (± 5.4)	-23.2 (± 5.1)	-51.3 (± 4.8)	

Statistical analyses

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0228
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-17.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.8
upper limit	-2.4
Variability estimate	Standard error of the mean
Dispersion value	7.5

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-45.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.6
upper limit	-31
Variability estimate	Standard error of the mean
Dispersion value	7.3

Secondary: Percent Change from Baseline in Lipoprotein a [Lp(a)] at Week 16 (ITT Estimand)

End point title	Percent Change from Baseline in Lipoprotein a [Lp(a)] at Week 16 (ITT Estimand)
End point description:	

End point type	Secondary
End point timeframe:	
Baseline and Week 16	

End point values	Group A: Placebo SC QW (DBTP)	Group A: Evinacumab 300mg SC Q2W (DBTP)	Group A: Evinacumab 300mg SC QW (DBTP)	Group A: Evinacumab 450mg SC QW (DBTP)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	39	39	42	40
Units: Percent Change				
least squares mean (standard error)	0.3 (± 3.9)	-10.3 (± 4.1)	-11.6 (± 4.0)	-8.9 (± 4.0)

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	0.8 (± 3.7)	-15.7 (± 3.7)	-15.7 (± 3.3)	

Statistical analyses

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC Q2W (DBTP)
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0635
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-10.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.8
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	5.7

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 300mg SC QW (DBTP)
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0314
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.8
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	5.5

Statistical analysis title	Week 16
Comparison groups	Group A: Placebo SC QW (DBTP) v Group A: Evinacumab 450mg SC QW (DBTP)
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0923
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-9.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.9
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	5.5

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0017
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-16.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.8
upper limit	-6.2
Variability estimate	Standard error of the mean
Dispersion value	5.3

Statistical analysis title	Week 16
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0009
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-16.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.2
upper limit	-6.8
Variability estimate	Standard error of the mean
Dispersion value	4.9

Secondary: Percent Change from Baseline in Lipoprotein (a) [Lp(a)] at Week 24 (ITT Estimand)

End point title	Percent Change from Baseline in Lipoprotein (a) [Lp(a)] at Week 24 (ITT Estimand)[7]

End point description:

End point type	Secondary

End point timeframe:

Baseline and Week 24

Notes:

[7] - 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: This endpoint is only applicable to those patients receiving IV route of study treatment administration

End point values	Group B: Placebo IV Q4W (DBTP)	Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	35	38	
Units: Percent Change				
least squares mean (standard error)	-1.4 (± 4.1)	-17.5 (± 4.0)	-16.0 (± 3.7)	

Statistical analyses

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 5mg/kg IV Q4W (DBTP)
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0054
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-16.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.4
upper limit	-4.7
Variability estimate	Standard error of the mean
Dispersion value	5.8

Statistical analysis title	Week 24
Comparison groups	Group B: Placebo IV Q4W (DBTP) v Group B: Evinacumab 15mg/kg IV Q4W (DBTP)

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0085
Method	Regression, Linear
Parameter estimate	Adjusted Mean Difference
Point estimate	-14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.4
upper limit	-3.7
Variability estimate	Standard error of the mean
Dispersion value	5.5

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From day of first treatment until the end of study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22

Reporting groups	
Reporting group title	DB Evinacumab 5 mg
Reporting group description:	
Group B: Evinacumab 5mg/kg IV Q4W (DBTP)	
Reporting group title	DB Placebo IV Q4W (DBTP)
Reporting group description:	
Group B: Placebo IV Q4W (DBTP)	
Reporting group title	DB Placebo IV Q4W (OLTP)
Reporting group description:	
Group B: DB Placebo IV Q4W (OLTP)	
Reporting group title	DB Evinacumab 15 mg
Reporting group description:	
Group B: Evinacumab 15mg/kg IV Q4W (DBTP)	
Reporting group title	DB Evinacumab 5 mg/kg IV Q4W (OLTP)
Reporting group description:	
Group B: DB Evinacumab 5mg/kg IV Q4W (OLTP)	
Reporting group title	DB Evinacumab 15 mg/kg IV Q4W (OLTP)
Reporting group description:	
Group B: DB Evinacumab 15mg/kg IV Q4W (OLTP)	
Reporting group title	DB Placebo SC QW (DBTP)
Reporting group description:	
Group A: Placebo SC QW (DBTP)	
Reporting group title	DB Evinacumab 300 mg SC Q2W (DBTP)
Reporting group description:	
Group A: Evinacumab 300mg SC Q2W (DBTP)	
Reporting group title	DB Evinacumab 300 mg SC QW (DBTP)
Reporting group description:	
Group A: Evinacumab 300mg SC QW (DBTP)	
Reporting group title	DB Evinacumab 450 mg SC QW (DBTP)
Reporting group description:	
Group A: Evinacumab 450mg SC QW (DBTP)	

Serious adverse events	DB Evinacumab 5 mg	DB Placebo IV Q4W (DBTP)	DB Placebo IV Q4W (OLTP)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 36 (5.56%)	1 / 33 (3.03%)	4 / 31 (12.90%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			

Acquired hydrocele			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 31 (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
Dyspnoea			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (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
Tibia fracture			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (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
Palpitations			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (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 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (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			
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder polyp			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DB Evinacumab 15 mg	DB Evinacumab 5 mg/kg IV Q4W (OLTP)	DB Evinacumab 15 mg/kg IV Q4W (OLTP)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 37 (16.22%)	3 / 32 (9.38%)	2 / 33 (6.06%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			

subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (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			
Chest pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (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
General physical health deterioration			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (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
Reproductive system and breast disorders			
Acquired hydrocele			

subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (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
Pulmonary embolism			
subjects affected / exposed	0 / 37 (0.00%)	1 / 32 (3.13%)	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			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (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
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			

subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (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 disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (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
Palpitations			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (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
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 37 (0.00%)	1 / 32 (3.13%)	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
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder polyp			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 32 (3.13%)	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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DB Placebo SC QW (DBTP)	DB Evinacumab 300 mg SC Q2W (DBTP)	DB Evinacumab 300 mg SC QW (DBTP)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 39 (7.69%)	2 / 39 (5.13%)	4 / 42 (9.52%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			

subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Acquired hydrocele			

subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			

subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive encephalopathy			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 42 (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
Syncope			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary bladder polyp			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DB Evinacumab 450 mg SC QW (DBTP)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 40 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glioblastoma			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transitional cell carcinoma			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Acquired hydrocele			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Rib fracture			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive encephalopathy			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary bladder polyp			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Corona virus infection			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)		
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	DB Evinacumab 5 mg	DB Placebo IV Q4W (DBTP)	DB Placebo IV Q4W (OLTP)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 36 (63.89%)	18 / 33 (54.55%)	19 / 31 (61.29%)
Vascular disorders			

Hypertension			
subjects affected / exposed	3 / 36 (8.33%)	1 / 33 (3.03%)	1 / 31 (3.23%)
occurrences (all)	3	1	1
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	3 / 36 (8.33%)	3 / 33 (9.09%)	1 / 31 (3.23%)
occurrences (all)	3	3	1
Fatigue			
subjects affected / exposed	4 / 36 (11.11%)	2 / 33 (6.06%)	3 / 31 (9.68%)
occurrences (all)	4	2	3
Asthenia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	3 / 31 (9.68%)
occurrences (all)	1	0	3
Injection site bruising			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	10	0	0
Injection site haematoma			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			

subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	1 / 31 (3.23%)
occurrences (all)	0	2	1
Epistaxis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Oropharyngeal pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2

Body temperature increased			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 36 (5.56%)	6 / 33 (18.18%)	4 / 31 (12.90%)
occurrences (all)	3	10	4
Dizziness			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	3	0	0
Lethargy			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Dyspepsia			
subjects affected / exposed	1 / 36 (2.78%)	2 / 33 (6.06%)	1 / 31 (3.23%)
occurrences (all)	1	2	1
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 36 (0.00%)	2 / 33 (6.06%)	1 / 31 (3.23%)
occurrences (all)	0	2	1
Abdominal discomfort			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Abdominal pain upper			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	3	0	0
Constipation			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	5 / 36 (13.89%)	4 / 33 (12.12%)	2 / 31 (6.45%)
occurrences (all)	5	5	3
Arthralgia			
subjects affected / exposed	2 / 36 (5.56%)	3 / 33 (9.09%)	3 / 31 (9.68%)
occurrences (all)	2	3	3
Back pain			
subjects affected / exposed	3 / 36 (8.33%)	2 / 33 (6.06%)	2 / 31 (6.45%)
occurrences (all)	3	2	4
Musculoskeletal pain			

subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	3 / 36 (8.33%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	3	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 36 (8.33%)	2 / 33 (6.06%)	5 / 31 (16.13%)
occurrences (all)	4	2	7
Gastroenteritis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 33 (3.03%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Influenza			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 36 (2.78%)	0 / 33 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2

Urinary tract infection			
subjects affected / exposed	2 / 36 (5.56%)	0 / 33 (0.00%)	2 / 31 (6.45%)
occurrences (all)	3	0	2
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 36 (8.33%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	3	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 36 (0.00%)	0 / 33 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	DB Evinacumab 15 mg	DB Evinacumab 5 mg/kg IV Q4W (OLTP)	DB Evinacumab 15 mg/kg IV Q4W (OLTP)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 37 (64.86%)	22 / 32 (68.75%)	24 / 33 (72.73%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 37 (2.70%)	3 / 32 (9.38%)	4 / 33 (12.12%)
occurrences (all)	2	4	5
Fatigue			
subjects affected / exposed	1 / 37 (2.70%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Asthenia			
subjects affected / exposed	3 / 37 (8.11%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	3	0	0
Chest pain			
subjects affected / exposed	2 / 37 (5.41%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
Injection site bruising			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			

subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 37 (2.70%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Epistaxis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 37 (2.70%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
Oropharyngeal pain			

subjects affected / exposed	0 / 37 (0.00%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 37 (0.00%)	2 / 32 (6.25%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Depression			
subjects affected / exposed	1 / 37 (2.70%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	1 / 33 (3.03%)
occurrences (all)	0	0	1
Body temperature increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 37 (0.00%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	0 / 37 (0.00%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 37 (13.51%)	2 / 32 (6.25%)	4 / 33 (12.12%)
occurrences (all)	6	2	6
Dizziness			

subjects affected / exposed	3 / 37 (8.11%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	3	1	0
Lethargy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 37 (0.00%)	3 / 32 (9.38%)	1 / 33 (3.03%)
occurrences (all)	0	4	1
Dyspepsia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 37 (2.70%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	1	1	0
Abdominal discomfort			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	2 / 37 (5.41%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	5	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 37 (0.00%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 37 (8.11%)	1 / 32 (3.13%)	1 / 33 (3.03%)
occurrences (all)	3	1	1
Toothache			

subjects affected / exposed	0 / 37 (0.00%)	1 / 32 (3.13%)	1 / 33 (3.03%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	2 / 37 (5.41%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	2	1	0
Arthralgia			
subjects affected / exposed	1 / 37 (2.70%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Back pain			
subjects affected / exposed	2 / 37 (5.41%)	3 / 32 (9.38%)	0 / 33 (0.00%)
occurrences (all)	2	3	0
Musculoskeletal pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 37 (5.41%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 37 (16.22%)	4 / 32 (12.50%)	3 / 33 (9.09%)
occurrences (all)	6	4	4
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 32 (6.25%)	2 / 33 (6.06%)
occurrences (all)	0	3	2
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	3 / 32 (9.38%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
Cystitis			

subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
Oral herpes			
subjects affected / exposed	0 / 37 (0.00%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Respiratory tract infection			
subjects affected / exposed	1 / 37 (2.70%)	0 / 32 (0.00%)	3 / 33 (9.09%)
occurrences (all)	1	0	4
Sinusitis			
subjects affected / exposed	1 / 37 (2.70%)	2 / 32 (6.25%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 37 (2.70%)	3 / 32 (9.38%)	3 / 33 (9.09%)
occurrences (all)	1	4	3
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	6 / 32 (18.75%)	3 / 33 (9.09%)
occurrences (all)	0	8	7
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 37 (0.00%)	0 / 32 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 37 (0.00%)	1 / 32 (3.13%)	0 / 33 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	DB Placebo SC QW (DBTP)	DB Evinacumab 300 mg SC Q2W (DBTP)	DB Evinacumab 300 mg SC QW (DBTP)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 39 (51.28%)	27 / 39 (69.23%)	26 / 42 (61.90%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			

Influenza like illness			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	3 / 39 (7.69%)	0 / 39 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
Asthenia			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	3 / 42 (7.14%)
occurrences (all)	0	1	4
Injection site bruising			
subjects affected / exposed	2 / 39 (5.13%)	1 / 39 (2.56%)	1 / 42 (2.38%)
occurrences (all)	11	1	2
Injection site erythema			
subjects affected / exposed	1 / 39 (2.56%)	2 / 39 (5.13%)	1 / 42 (2.38%)
occurrences (all)	4	2	4
Injection site haematoma			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	3 / 42 (7.14%)
occurrences (all)	2	0	5
Injection site haemorrhage			
subjects affected / exposed	1 / 39 (2.56%)	1 / 39 (2.56%)	3 / 42 (7.14%)
occurrences (all)	1	6	3
Injection site pain			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	1 / 42 (2.38%)
occurrences (all)	0	6	2
Injection site reaction			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1

Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 39 (5.13%)	1 / 39 (2.56%)	3 / 42 (7.14%)
occurrences (all)	2	1	3
Epistaxis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	2 / 42 (4.76%)
occurrences (all)	0	1	2
Oropharyngeal pain			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	4 / 42 (9.52%)
occurrences (all)	2	0	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences (all)	2	0	1
Insomnia			
subjects affected / exposed	1 / 39 (2.56%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	1 / 39 (2.56%)	2 / 39 (5.13%)	1 / 42 (2.38%)
occurrences (all)	1	2	1
Fall			
subjects affected / exposed	1 / 39 (2.56%)	0 / 39 (0.00%)	4 / 42 (9.52%)
occurrences (all)	1	0	4
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 39 (10.26%)	2 / 39 (5.13%)	3 / 42 (7.14%)
occurrences (all)	7	2	5
Dizziness			
subjects affected / exposed	5 / 39 (12.82%)	1 / 39 (2.56%)	2 / 42 (4.76%)
occurrences (all)	6	1	2
Lethargy			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	2 / 42 (4.76%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 39 (7.69%)	1 / 39 (2.56%)	2 / 42 (4.76%)
occurrences (all)	5	2	3
Dyspepsia			
subjects affected / exposed	1 / 39 (2.56%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Abdominal discomfort			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0

Abdominal pain			
subjects affected / exposed	4 / 39 (10.26%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	4	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 39 (2.56%)	4 / 39 (10.26%)	0 / 42 (0.00%)
occurrences (all)	1	4	0
Nausea			
subjects affected / exposed	3 / 39 (7.69%)	4 / 39 (10.26%)	1 / 42 (2.38%)
occurrences (all)	3	4	1
Toothache			
subjects affected / exposed	2 / 39 (5.13%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 39 (0.00%)	4 / 39 (10.26%)	1 / 42 (2.38%)
occurrences (all)	0	5	3
Arthralgia			
subjects affected / exposed	1 / 39 (2.56%)	3 / 39 (7.69%)	1 / 42 (2.38%)
occurrences (all)	1	3	1
Back pain			
subjects affected / exposed	5 / 39 (12.82%)	3 / 39 (7.69%)	4 / 42 (9.52%)
occurrences (all)	6	3	5
Musculoskeletal pain			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	1 / 42 (2.38%)
occurrences (all)	0	2	2
Muscle spasms			
subjects affected / exposed	1 / 39 (2.56%)	2 / 39 (5.13%)	1 / 42 (2.38%)
occurrences (all)	1	4	4
Pain in extremity			

subjects affected / exposed	2 / 39 (5.13%)	2 / 39 (5.13%)	1 / 42 (2.38%)
occurrences (all)	2	2	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 39 (15.38%)	4 / 39 (10.26%)	4 / 42 (9.52%)
occurrences (all)	7	5	5
Gastroenteritis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	1 / 42 (2.38%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 39 (0.00%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	2 / 42 (4.76%)
occurrences (all)	0	0	2
Influenza			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	1 / 42 (2.38%)
occurrences (all)	0	2	1
Oral herpes			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 39 (0.00%)	2 / 39 (5.13%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	2 / 42 (4.76%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	4 / 39 (10.26%)	5 / 39 (12.82%)	5 / 42 (11.90%)
occurrences (all)	7	6	6
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	0 / 42 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	2 / 39 (5.13%)	1 / 39 (2.56%)	0 / 42 (0.00%)
occurrences (all)	2	1	0

Non-serious adverse events	DB Evinacumab 450 mg SC QW (DBTP)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 40 (55.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	15		
Asthenia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Injection site bruising			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	26		
Injection site haematoma			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Injection site haemorrhage			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Nasal congestion			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Depression			

subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Body temperature increased			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Dizziness			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Lethargy			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	 3 / 40 (7.50%) 17 0 / 40 (0.00%) 0 1 / 40 (2.50%) 2 2 / 40 (5.00%) 2 0 / 40 (0.00%) 0 0 / 40 (0.00%) 0 0 / 40 (0.00%) 0 4 / 40 (10.00%) 21 0 / 40 (0.00%) 0		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 0 / 40 (0.00%) 0		
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2			
Arthralgia subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3			
Back pain subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2			
Musculoskeletal pain subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 4			
Muscle spasms subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 4			
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 40 (10.00%) 6			
Gastroenteritis subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3			
Bronchitis subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1			
Cystitis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0			
Influenza subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0			
Oral herpes				

subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Respiratory tract infection			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	6		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2017	Amendment 1: The protocol is amended primarily to update post-dose monitoring to standardize across the evinacumab program.
29 September 2017	Amendment 2: Specified that enrollment of intravenous (IV) cohorts will precede enrollment of subcutaneous (SC) cohorts.
01 March 2018	Amendment 3: Added a 24-week open-label treatment period after the 24-week double-blind treatment period for the IV groups. The purpose of this change was to obtain long term safety information with continuous exposure of evinacumab IV for up to 48 weeks. As a result, the mandatory 24-week follow up period for the IV treatment groups was removed to allow patients to go directly into a separate OL study after completing the double-blind treatment period and open label treatment period. Patients who do not participate in the OL study would enter a 24-week follow up period.
09 October 2018	Amendment 4: major changes include increasing the duration of the open-label treatment period for Group B from 24 weeks to 48 weeks
11 October 2019	Amendment 5: The protocol was amended in response to recent nonclinical findings

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported