Clinical trial results:
A Phase 2, Randomized, Placebo-Controlled Study of Safety and Efficacy, Following Repeat-Dose Administration of Evinacumab (anti-ANGPTL3) in Patients with Severe Hypertriglyceridemia (sHTG) at Risk for Acute Pancreatitis

Summary

EudraCT number	2016-003307-62
Trial protocol	GB IT
Global end of trial date	23 July 2020

Results information

Result version number	v1 (current)
This version publication date	06 August 2021
First version publication date	06 August 2021

Trial information

Trial identification

Sponsor protocol code	R1500-HTG-1522

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03452228
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, NY, United States, 10591
Public contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com
Scientific contact	Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, 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	23 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objectives: Determine change in triglyceride (TG) levels following 12 wks of repeated intravenous (IV) doses of evinacumab in subset of subjects with a documented history of sHTG (TG ≥1000 milligrams per decilter (mg/dL), a TG level of at least 500 mg/dL at screening, a history of acute pancreatitis & w/out loss-of-function (LOF) mutations in genes in lipoprotein lipase (LPL) pathway; Assess whether reduction in TG of at least 40% from baseline placebo period was achieved. Secondary objectives: Determine percent change from baseline in TG levels following evinacumab overall & in subgroups; Assess changes in reported abdominal/gastrointestinal (GI) symptoms, dietary habits, & symptom/dietary impact measures; Assess degree of pancreatic injury/inflammation at baseline & following 12 & 24 wks of treatment; Evaluate total evinacumab, total ANGPTL3, & anti-drug antibody (ADA) during evinacumab treatment & follow-up periods; Evaluate safety & tolerability of evinacumab

Protection of trial subjects:

It is the responsibility of both the sponsor and the investigator(s) to ensure that this clinical study will be 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 GCP and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2018
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	Canada: 11
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	United States: 30
Worldwide total number of subjects	52
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	50
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 17 centers enrolled subjects in Italy, Canada, United Kingdom of Great Britain and Northern Ireland, and United States.

Pre-assignment

Screening details:

The study consisted of a screening period of up to 37 days.

Period 1

Period 1 title	12-week double-blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Placebo IV Q4W/SB Evinacumab

Arm description:

Subjects received placebo matching evinacumab intravenously (IV) every 4 weeks (Q4W) on days 1, 29, and 57 during the 12-week double-blind treatment period (DBTP). During the 12-week single-blind treatment period (SBTP), subjects received evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) placebo

Arm title	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab

Arm description:

Subjects received evinacumab 15 mg/kg IV Q4W on days 1, 29, and 57 during the 12-week DBTP. During the 12-week SBTP, subjects continued to receive evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	REGN1500
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) evinacumab

Number of subjects in period 1	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab
Started	17	35
Randomized and Treated	16	35
Completed	15	32
Not completed	2	3
Physician decision	1	-
Adverse event, non-fatal	-	2
Lost to follow-up	1	1

Period 2

Period 2 title	12-week single-blind
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Placebo/SB Evinacumab IV 15mg/kg Q4W

Arm description:

Subjects received placebo matching evinacumab intravenously (IV) every 4 weeks (Q4W) on days 1, 29, and 57 during the 12-week double-blind treatment period (DBTP). During the 12-week single-blind treatment period (SBTP), subjects received evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	REGN1500
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) evinacumab

Arm title	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W

Arm description:

Subjects received evinacumab 15 mg/kg IV Q4W on days 1, 29, and 57 during the 12-week DBTP. During the 12-week SBTP, subjects continued to receive evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.

Arm type	Experimental
Investigational medicinal product name	evinacumab
Investigational medicinal product code	REGN1500
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous (IV) evinacumab

Number of subjects in period 2	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Started	15	32
Completed SBTP	15	32
Completed off-treatment follow-up	14	29
Completed	14	29
Not completed	1	3
Consent withdrawn by subject	1	3

Baseline characteristics

Reporting groups	
Reporting group title	DB Placebo IV Q4W/SB Evinacumab
Reporting group description:	
Subjects received placebo matching evinacumab intravenously (IV) every 4 weeks (Q4W) on days 1, 29, and 57 during the 12-week double-blind treatment period (DBTP). During the 12-week single-blind treatment period (SBTP), subjects received evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Reporting group title	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab
Reporting group description:	
Subjects received evinacumab 15 mg/kg IV Q4W on days 1, 29, and 57 during the 12-week DBTP. During the 12-week SBTP, subjects continued to receive evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	

Reporting group values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	Total
Number of subjects	17	35	52
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)	15	35	50
From 65-84 years	2	0	2
85 years and over	0	0	0
Sex: Female, Male Units: Subjects			
Female	7	17	24
Male	10	18	28
Race Units: Subjects			
White	13	29	42
Black or African American	0	1	1
Asian	1	5	6
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
Not Reported	0	0	0
Other	3	0	3

End points reporting groups

Reporting group title	DB Placebo IV Q4W/SB Evinacumab
Reporting group description:	
Subjects received placebo matching evinacumab intravenously (IV) every 4 weeks (Q4W) on days 1, 29, and 57 during the 12-week double-blind treatment period (DBTP). During the 12-week single-blind treatment period (SBTP), subjects received evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Reporting group title	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab
Reporting group description:	
Subjects received evinacumab 15 mg/kg IV Q4W on days 1, 29, and 57 during the 12-week DBTP. During the 12-week SBTP, subjects continued to receive evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Reporting group title	DB Placebo/SB Evinacumab IV 15mg/kg Q4W
Reporting group description:	
Subjects received placebo matching evinacumab intravenously (IV) every 4 weeks (Q4W) on days 1, 29, and 57 during the 12-week double-blind treatment period (DBTP). During the 12-week single-blind treatment period (SBTP), subjects received evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Reporting group title	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Reporting group description:	
Subjects received evinacumab 15 mg/kg IV Q4W on days 1, 29, and 57 during the 12-week DBTP. During the 12-week SBTP, subjects continued to receive evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Subject analysis set title	Actual Cohort 1 DB Placebo IV Q4W/SB evinacumab
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Actual Cohort 1 (DBTP 12 weeks placebo; SBTP 12 weeks evinacumab) includes subjects with homozygous or compound heterozygous loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data.	
Subject analysis set title	Actual Cohort 1 DB/SB Evinacumab IV 15mg/kg Q4W
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Actual Cohort 1 (DBTP/SBTP evinacumab) includes subjects with homozygous or compound heterozygous loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data.	
Subject analysis set title	Actual Cohort 2 DB Placebo IV Q4W/SB evinacumab
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Actual Cohort 2 (DBTP 12 weeks placebo; SBTP 12 weeks evinacumab) includes subjects with heterozygous loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data.	
Subject analysis set title	Actual Cohort 2 DB/SB Evinacumab IV 15mg/kg Q4W
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Actual Cohort 2 (DBTP/SBTP evinacumab) includes subjects with heterozygous loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data.	
Subject analysis set title	Actual Cohort 3 DB Placebo IV Q4W/SB evinacumab
Subject analysis set type	Full analysis
Subject analysis set description:	
Actual Cohort 3 (DBTP 12 weeks placebo; SBTP 12 weeks evinacumab) includes subjects without loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data.	
Subject analysis set title	Actual Cohort 3 DB/SB Evinacumab IV 15mg/kg Q4W
Subject analysis set type	Full analysis
Subject analysis set description:	
Actual Cohort 3 (DBTP/SBTP evinacumab) includes subjects without loss-of-function (LOF) mutations in	

genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data.

Primary: Percent lowering of triglyceride (TG) levels from baseline following 12 weeks of repeated IV doses of evinacumab (Actual Cohort 3)

End point title	Percent lowering of triglyceride (TG) levels from baseline following 12 weeks of repeated IV doses of evinacumab (Actual Cohort 3)

End point description:

Actual cohort 3 includes subjects without loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data. All subjects included received 12 weeks of evinacumab treatment, regardless of DBTP treatment assignment. For subjects randomized to evinacumab treatment group, baseline (Week 0) was defined as the geometric mean of all available TG results at day -28, day -14 and week 0; for subjects randomized to placebo treatment group, baseline (Week 12) was defined as the geometric mean of all available TG results at weeks 6, 8, and 12. Full analysis set (FAS) includes all randomized subjects who received any double-blind/single-blind study drug; Mixed-effect repeated measures model (MMRM) analysis

End point type	Primary

End point timeframe:

12 weeks

End point values	Actual Cohort 3 DB Placebo IV Q4W/SB evinacumab	Actual Cohort 3 DB/SB Evinacumab IV 15mg/kg Q4W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	14		
Units: Percent Change				
least squares mean (standard error)	19.2 (± 99.1)	-37.2 (± 42.9)		

Statistical analyses

Statistical analysis title	SB Evinacumab, DB Evinacumab

Statistical analysis description:

Mixed-effect repeated measures model (MMRM) analyzed subject's natural log transformation TG ratio (each evinacumab treatment visit/baseline) with the fixed categorical effects of evinacumab treatment visit (i.e. exposed to evinacumab visits only), actual cohort, and evinacumab treatment visit by actual cohort interaction, as well as the continuous covariates of the log transformation of baseline TG and the log transformation of baseline TG by evinacumab treatment visit interaction.

Comparison groups	Actual Cohort 3 DB/SB Evinacumab IV 15mg/kg Q4W v Actual Cohort 3 DB Placebo IV Q4W/SB evinacumab
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least Squares (LS) Mean
Point estimate	-27.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.2
upper limit	84.6

Variability estimate	Standard error of the mean
Dispersion value	37.4

Secondary: Percent TG lowering from baseline following 12 weeks of repeated IV doses of evinacumab (Actual Cohort 2)

End point title	Percent TG lowering from baseline following 12 weeks of repeated IV doses of evinacumab (Actual Cohort 2)

End point description:

Actual cohort 2 includes subjects with heterozygous loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data. All subjects included received 12 weeks of evinacumab treatment, regardless of DBTP treatment assignment. For subjects randomized to evinacumab treatment group, baseline (Week 0) was defined as the geometric mean of all available TG results at day -28, day -14 and week 0; for subjects randomized to placebo treatment group, baseline (Week 12) was defined as the geometric mean of all available TG results at weeks 6, 8, and 12. Full analysis set (FAS) includes all randomized subjects who received any double-blind/single-blind study drug; Mixed-effect repeated measures model (MMRM) analysis

End point type	Secondary

End point timeframe:

12 weeks

End point values	Actual Cohort 2 DB Placebo IV Q4W/SB evinacumab	Actual Cohort 2 DB/SB Evinacumab IV 15mg/kg Q4W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	9		
Units: Percent Change				
least squares mean (standard error)	-45.1 (± 41.6)	-16.3 (± 66.2)		

Statistical analyses

Statistical analysis title	SB evinacumab, DB evinacumab

Statistical analysis description:

Mixed-effect repeated measures model (MMRM) analyzed subject's natural log transformation TG ratio (each evinacumab treatment visit/baseline) with the fixed categorical effects of evinacumab treatment visit (i.e. exposed to evinacumab visits only), actual cohort, and evinacumab treatment visit by actual cohort interaction, as well as the continuous covariates of the log transformation of baseline TG and the log transformation of baseline TG by evinacumab treatment visit interaction.

Comparison groups	Actual Cohort 2 DB Placebo IV Q4W/SB evinacumab v Actual Cohort 2 DB/SB Evinacumab IV 15mg/kg Q4W
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least Squares (LS) Mean
Point estimate	-30.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.4
upper limit	90.7
Variability estimate	Standard error of the mean
Dispersion value	38.1

Secondary: Percent TG lowering from baseline following 12 weeks of repeated IV doses of evinacumab (Actual Cohort 1)

End point title	Percent TG lowering from baseline following 12 weeks of repeated IV doses of evinacumab (Actual Cohort 1)

End point description:

Actual cohort 1 includes subjects with homozygous or compound heterozygous loss-of-function (LOF) mutations in genes in the lipoprotein lipase (LPL) pathway as was determined based on genotype data. All subjects included received 12 weeks of evinacumab treatment, regardless of DBTP treatment assignment. For subjects randomized to evinacumab treatment group, baseline (Week 0) was defined as the geometric mean of all available TG results at day -28, day -14 and week 0; for subjects randomized to placebo treatment group, baseline (Week 12) was defined as the geometric mean of all available TG results at weeks 6, 8, and 12. Full analysis set (FAS) includes all randomized subjects who received any double-blind/single-blind study drug; Mixed-effect repeated measures model (MMRM) analysis; 99999=not evaluable

End point type	Secondary

End point timeframe:

12 weeks

End point values	Actual Cohort 1 DB Placebo IV Q4W/SB evinacumab	Actual Cohort 1 DB/SB Evinacumab IV 15mg/kg Q4W		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	12		
Units: Percent Change				
least squares mean (standard error)	99999 (± 99999)	-25.7 (± 26.6)		

Statistical analyses

Statistical analysis title	SB evinacumab, DB evinacumab

Statistical analysis description:

Mixed-effect repeated measures model (MMRM) analyzes patient’s natural log transformation TG ratio (each evinacumab treatment visit/baseline) with the fixed categorical effects of evinacumab treatment visit (i.e. exposed to evinacumab visits only), as well as the continuous covariates of the log transformation of baseline TG and the log transformation of baseline TG by evinacumab treatment visit interaction.

Comparison groups	Actual Cohort 1 DB Placebo IV Q4W/SB evinacumab v Actual Cohort 1 DB/SB Evinacumab IV 15mg/kg Q4W

Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Least Squares (LS) Mean
Point estimate	-31.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.2
upper limit	34
Variability estimate	Standard error of the mean
Dispersion value	22.4

Secondary: Percent TG lowering from baseline following 2 to 24 weeks of repeated IV doses of evinacumab (Actual Cohorts 1,2, and 3)

End point title	Percent TG lowering from baseline following 2 to 24 weeks of repeated IV doses of evinacumab (Actual Cohorts 1,2, and 3)

End point description:

Includes subjects initially randomized to evinacumab per cohort during the DBTP (FAS DBTP and SBTP); Actual cohort was determined based on genotype data. Baseline fasting TG is defined as the mean of the last 2 measurements during the placebo run-in (day -28, day -14) and week 0; n=number of subjects evaluable at that time point.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Actual Cohort 1 DB/SB Evinacumab IV 15mg/kg Q4W	Actual Cohort 2 DB/SB Evinacumab IV 15mg/kg Q4W	Actual Cohort 3 DB/SB Evinacumab IV 15mg/kg Q4W	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	11	9	12	
Units: Percent Change				
median (inter-quartile range (Q1-Q3))				
Week 2 (n=11, 9, 11)	-28.3 (-40.3 to -6.5)	-77.5 (-81.2 to -58.9)	-74.4 (-84.2 to -37.1)	
Week 4 (n=11, 9, 12)	-19.0 (-69.6 to -2.7)	-48.0 (-76.2 to -29.2)	-70.3 (-83.4 to -50.2)	
Week 6 (n=11, 9, 11)	-47.1 (-59.1 to -5.6)	-84.6 (-85.7 to -61.3)	-71.3 (-87.0 to -39.5)	
Week 8 (n=11, 9, 12)	-29.5 (-72.0 to 4.8)	-69.2 (-72.2 to -58.4)	-62.5 (-84.8 to 48.0)	
Week 12 (n=11, 9, 12)	-27.7 (-68.5 to 2.2)	-64.8 (-84.5 to -41.8)	-81.7 (-90.5 to -21.7)	
Week 16 (n=11, 9, 12)	-16.2 (-56.7 to 29.3)	-71.3 (-80.8 to -57.1)	-80.4 (-87.2 to -37.3)	
Week 20 (n=11, 9, 12)	-37.2 (-49.9 to -8.8)	-65.5 (-70.2 to -45.8)	-75.7 (-88.1 to -6.6)	
Week 24 (n=11, 9, 12)	-7.7 (-31.8 to 9.1)	-75.7 (-82.3 to -57.1)	-71.4 (-86.5 to -54.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent TG lowering from baseline following 2 to 24 weeks of repeated IV doses of evinacumab overall

End point title	Percent TG lowering from baseline following 2 to 24 weeks of repeated IV doses of evinacumab overall[1]

End point description:

Percent TG lowering from baseline following 2 to 24 weeks of repeated IV doses of evinacumab in subjects randomized to evinacumab during the DBTP. Baseline fasting TG is defined as the mean of the last 2 measurements during the placebo run-in (day -28, day -14) and week 0; n=number of subjects evaluable at that time point; 99999=not applicable to treatment period; Double-blind safety analysis set: Randomized population who received at least 1 dose or part of a dose of double-blind study drug; Single-blind safety analysis set: Randomized population who received at least 1 dose or part of a dose of single-blind study drug

End point type	Secondary

End point timeframe:

Up to 24 weeks

Notes:

[1] - 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: Endpoint includes only subjects randomized to evinacumab treatment group.

End point values	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35[2]	32[3]		
Units: Percent Change				
median (inter-quartile range (Q1-Q3))				
Week 2 (n=31)	-58.86 (-78.62 to -27.62)	99999 (99999 to 99999)		
Week 4 (n=32)	-48.60 (-77.35 to -14.40)	99999 (99999 to 99999)		
Week 6 (n=31)	-61.25 (-85.38 to -39.51)	99999 (99999 to 99999)		
Week 8 (n=32)	-60.08 (-80.96 to -3.14)	99999 (99999 to 99999)		
Week 12 (n=32)	-56.59 (-87.09 to -12.34)	99999 (99999 to 99999)		
Week 16 (n=32)	99999 (99999 to 99999)	-63.10 (-82.83 to -15.47)		
Week 20 (n=32)	99999 (99999 to 99999)	-47.86 (-82.53 to -21.52)		
Week 24 (n=32)	99999 (99999 to 99999)	-57.90 (-83.85 to -6.24)		

Notes:

[2] - Double-Blind Safety Analysis Set - DBTP

[3] - Single-Blind Safety Analysis Set - SBTP

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in subject reported abdominal and gastrointestinal symptoms scale

End point title	Change from baseline in subject reported abdominal and gastrointestinal symptoms scale

End point description:

Abdominal and gastrointestinal (GI) daily symptoms were assessed using the Hypertriglyceridemia and Acute Pancreatitis Symptom Scale (HAP-SS), a 19-item measure of symptoms that has a 24-hour recall period and consists of a total score and four domain scores: pain; abdominal symptoms; physical symptoms; other symptoms, each scored 0 (no symptoms) to 100 (severe symptoms). Patient-reported outcomes (PRO) analysis set: all randomized subjects who received any double-blind study treatment with a baseline and at least 1 non-missing post-baseline PRO evaluation; n=number of subjects evaluable at that time point; 99999=not applicable to treatment period

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	9	23	19
Units: Score on a Scale				
arithmetic mean (standard deviation)				
Week 12 (DBTP) n=12; n=23	-0.69 (± 6.930)	99999 (± 99999)	-0.74 (± 5.102)	99999 (± 99999)
Week 24 (SBTP) n=9; n=19	99999 (± 99999)	-2.47 (± 5.860)	99999 (± 99999)	1.00 (± 4.319)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in patient reported daily dietary habits and impact questionnaire

End point title	Change from baseline in patient reported daily dietary habits and impact questionnaire

End point description:

Dietary habits and impact were measured by the Hypertriglyceridemia and Acute Pancreatitis Dietary

Behavior (HAP-DB), a 6-item measure of dietary behavior that has a 24-hour recall period using a 5-point frequency Likert scale (1=None of the time to 5=All of the time) and a dietary impact total score, ranging from 6 (no impact) to 30 (severe impact). Patient-reported outcomes (PRO) analysis set: all randomized subjects who received any double-blind study treatment with a baseline and at least 1 non-missing post-baseline PRO evaluation. n=number of subjects evaluable at that time point; 99999=not applicable to treatment period

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	29	30
Units: Scores on a Scale				
arithmetic mean (standard deviation)				
Week 12 (DBTP) n=12; n=23	-2.267 (± 5.5897)	99999 (± 99999)	2.021 (± 15.2152)	99999 (± 99999)
Week 24 (SBTP) n=9; n=19	99999 (± 99999)	-2.519 (± 6.4489)	99999 (± 99999)	-0.656 (± 8.4428)

Statistical analyses

No statistical analyses for this end point

Secondary: Degree of pancreatic injury/inflammation through 18^F-2-Fluoro-2-Deoxy-D Glucose positron emission tomography (18^F-FDG PET): maximum Standardized Uptake Value (SUVmax) at baseline (DBTP only)

End point title	Degree of pancreatic injury/inflammation through 18^F-2-Fluoro-2-Deoxy-D Glucose positron emission tomography (18^F-FDG PET): maximum Standardized Uptake Value (SUVmax) at baseline (DBTP only)

End point description:

PET analysis set: All randomized subjects who received any double-blind study treatment with a baseline and a post-baseline PET evaluation; PET imaging performed during the DBTP only (per protocol).

End point type	Secondary

End point timeframe:

Baseline

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	25		
Units: gram/milliliter (g/ml)				
arithmetic mean (standard deviation)	2.318 (± 0.6168)	2.738 (± 0.6027)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in degree of pancreatic injury/inflammation through 18^F-FDG-PET: SUVmax following 12 weeks of treatment with evinacumab (DBTP only)

End point title	Change from baseline in degree of pancreatic injury/inflammation through 18^F-FDG-PET: SUVmax following 12 weeks of treatment with evinacumab (DBTP only)

End point description:

PET analysis set: All randomized subjects who received any double-blind study treatment with a baseline and a post-baseline PET evaluation; PET imaging performed during the DBTP only (per protocol).

End point type	Secondary

End point timeframe:

Week 12

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	25		
Units: g/ml				
arithmetic mean (standard deviation)	0.576 (± 1.0628)	0.185 (± 0.5830)		

Statistical analyses

No statistical analyses for this end point

Secondary: Degree of pancreatic injury/inflammation through 18^F-FDG PET: SUVmean at baseline (DBTP only)

End point title	Degree of pancreatic injury/inflammation through 18^F-FDG PET: SUVmean at baseline (DBTP only)

End point description:

PET analysis set: All randomized subjects who received any double-blind study treatment with a baseline and a post-baseline PET evaluation; PET imaging performed during the DBTP only (per protocol).

End point type	Secondary

End point timeframe:

Baseline

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	25		
Units: g/ml				
arithmetic mean (standard deviation)	1.212 (± 0.2513)	1.478 (± 0.2000)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in degree of pancreatic injury/inflammation through 18^F-FDG PET: SUVmean following 12 weeks of treatment with evinacumab (DBTP only)

End point title	Change from baseline in degree of pancreatic injury/inflammation through 18^F-FDG PET: SUVmean following 12 weeks of treatment with evinacumab (DBTP only)

End point description:

PET analysis set: All randomized subjects who received any double-blind study treatment with a baseline and a post-baseline PET evaluation; PET imaging performed during the DBTP only (per protocol).

End point type	Secondary

End point timeframe:

Week 12

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	25		
Units: g/ml				
arithmetic mean (standard deviation)	0.175 (± 0.2117)	-0.007 (± 0.2312)		

Statistical analyses

No statistical analyses for this end point

Secondary: Degree of pancreatic injury/inflammation through Diffusion Weighted-Magnetic Resonance Imaging (DW-MRI) at baseline as assessed by apparent diffusion coefficient (ADC)

End point title	Degree of pancreatic injury/inflammation through Diffusion Weighted-Magnetic Resonance Imaging (DW-MRI) at baseline as assessed by apparent diffusion coefficient (ADC)

End point description:

MRI analysis set: All randomized subjects who received any double-blind study treatment with a baseline and at least 1 post-baseline MRI evaluation.

End point type	Secondary

End point timeframe:

Baseline (Week 0)

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	28		
Units: Square-millimeters per second (mm2/sec)				
arithmetic mean (standard deviation)	0.00144 (± 0.0003033)	0.00154 (± 0.000257)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to degree of pancreatic injury/inflammation through DW-MRI following 12 weeks of treatment with evinacumab as assessed by ADC (DBTP)

End point title	Change from baseline to degree of pancreatic injury/inflammation through DW-MRI following 12 weeks of treatment with evinacumab as assessed by ADC (DBTP)

End point description:

MRI analysis set: All randomized subjects who received any double-blind study treatment with a baseline and at least 1 post-baseline MRI evaluation.

End point type	Secondary

End point timeframe:

Week 12

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: mm2/sec				
arithmetic mean (standard deviation)	-0.00007 (± 0.000107)	0.00001 (± 0.00133)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to degree of pancreatic injury/inflammation through DW-MRI following 24 weeks of treatment with evinacumab as assessed by ADC (SBTP)

End point title	Change from baseline to degree of pancreatic injury/inflammation through DW-MRI following 24 weeks of treatment with evinacumab as assessed by ADC (SBTP)

End point description:

MRI analysis set: All randomized subjects who received any double-blind study treatment with a baseline and at least 1 post-baseline MRI evaluation.

End point type	Secondary

End point timeframe:

Week 24

End point values	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	24		
Units: mm2/sec				
arithmetic mean (standard deviation)	-0.00002 (± 0.000125)	0.00000 (± 0.000186)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total evinacumab concentration in serum

End point title	Total evinacumab concentration in serum

End point description:

Pharmacokinetic (PK) analysis set: All randomized subjects who received any study drug and have at least 1 non-missing measurement of evinacumab concentration following the first dose of the study drug. Double-blind treatment period (DBTP) is until week 12 Pre-Dose (PD); single-blind treatment period (SBTP) is from week 12 End of Infusion (EOI) until Week 24; n= number of subjects at each time point for each treatment group; 99999=not applicable to treatment period

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	35	32
Units: mg/L				
arithmetic mean (standard deviation)				
Week 4 PD (DBTP) n=14;n=31	0 (± 0)	99999 (± 99999)	73.6 (± 38.3)	99999 (± 99999)
Week 4 EOI (DBTP) n=14;n=30	0.334 (± 1.25)	99999 (± 99999)	590 (± 153)	99999 (± 99999)
Week 8 PD (DBTP) n=13;n=31	0 (± 0)	99999 (± 99999)	109 (± 57.2)	99999 (± 99999)
Week 8 EOI (DBTP) n=13;n=32	28.8 (± 104)	99999 (± 99999)	586 (± 119)	99999 (± 99999)
Week 12 PD (DBTP) n=14;n=31	0.00639 (± 0.0239)	99999 (± 99999)	124 (± 81.4)	99999 (± 99999)
Week 12 EOI (SBTP) n=13;n=32	99999 (± 99999)	544 (± 159)	99999 (± 99999)	662 (± 146)
Week 20 PD (SBTP) n=14;n=32	99999 (± 99999)	113 (± 51.9)	99999 (± 99999)	160 (± 119)
Week 20 EOI (SBTP) n=14;n=32	99999 (± 99999)	675 (± 146)	99999 (± 99999)	680 (± 199)
Week 24 (Post last dose 4 weeks) n=15;n=32	99999 (± 99999)	121 (± 76.7)	99999 (± 99999)	134 (± 77.2)
Week 28 (Post last dose 8 weeks) n=12;n=28	99999 (± 99999)	43.1 (± 47.8)	99999 (± 99999)	40.2 (± 44.6)
Week 36 (Post last dose 16 weeks) n=10;n=23	99999 (± 99999)	0.239 (± 0.250)	99999 (± 99999)	1.98 (± 7.41)
Week 44 (Post last dose 24 weeks) n=12;n=27	99999 (± 99999)	0.0190 (± 0.0464)	99999 (± 99999)	0.0680 (± 0.102)

Statistical analyses

No statistical analyses for this end point

Secondary: Total Angiopoietin-Like 3 (ANGPTL3) concentration in serum

End point title	Total Angiopoietin-Like 3 (ANGPTL3) concentration in serum

End point description:

Total target analysis set: All randomized subjects who received any study drug and have at least 1 non-missing measurement of total ANGPTL3 concentration following the first dose of study drug. Treatment assignments for the DBTP are based on the treatment received (placebo or evinacumab). Double-blind treatment period (DBTP) is until week 12 Pre-Dose (PD); single-blind treatment period (SBTP) is from week 12 End of Infusion (EOI) until Week 24; n= number of subjects at each time point for each treatment group; 99999=not applicable to treatment period

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	35	32
Units: mg/dL				
arithmetic mean (standard deviation)				
Week 4 PD (DBTP) n=14;n=31	0.111 (± 0.0272)	99999 (± 99999)	0.265 (± 0.0932)	99999 (± 99999)
Week 4 EOI (DBTP) n=14;n=30	0.106 (± 0.0205)	99999 (± 99999)	0.404 (± 0.132)	99999 (± 99999)
Week 8 PD (DBTP) n=13;n=31	0.114 (± 0.0333)	99999 (± 99999)	0.307 (± 0.0758)	99999 (± 99999)
Week 8 EOI (DBTP) n=13;n=32	0.137 (± 0.0977)	99999 (± 99999)	0.415 (± 0.0875)	99999 (± 99999)
Week 12 PD (DBTP) n=14;n=31	0.107 (± 0.0273)	99999 (± 99999)	0.310 (± 0.0911)	99999 (± 99999)
Week 12 EOI (SBTP) n=13;n=32	99999 (± 99999)	0.250 (± 0.0940)	99999 (± 99999)	0.394 (± 0.102)
Week 20 PD (SBTP) n=14;n=32	99999 (± 99999)	0.302 (± 0.0973)	99999 (± 99999)	0.346 (± 0.101)
Week 20 EOI (SBTP) n=14;n=32	99999 (± 999999)	0.407 (± 0.144)	99999 (± 99999)	0.422 (± 0.118)
Week 24 Post Last Dose 4 Weeks n=15;n=32	99999 (± 99999)	0.294 (± 0.0954)	99999 (± 99999)	0.331 (± 0.113)
Week 28 Post Last Dose 8 Weeks n=12;n=28	99999 (± 99999)	0.311 (± 0.0701)	99999 (± 99999)	0.265 (± 0.0984)
Week 36 Post Last Dose 16 Weeks n=10;n=23	99999 (± 99999)	0.134 (± 0.0487)	99999 (± 99999)	0.193 (± 0.0969)
Week 44 Post Last Dose 24 Weeks n=12;n=27	99999 (± 99999)	0.107 (± 0.0322)	99999 (± 99999)	0.131 (± 0.0489)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-Drug (evinacumab) Antibody (ADA)

End point title	Number of subjects with Anti-Drug (evinacumab) Antibody (ADA)

End point description:

ADA analysis set: All treated subjects who received any amount of study drug (active or placebo [safety analysis set]) and had at least 1 non-missing anti-evinacumab antibody result following the first dose of study drug or placebo. The ADA analysis set is based on the actual treatment received (as treated) rather than as randomized; Summary of ADA status ADA category by DBTP treatment group for Overall Study.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	34		
Units: Subjects				
number (not applicable)				
Negative any Time (Overall Study)	14	29		
Pre-existing Immunoreactivity (Overall Study)	1	4		
Treatment-Boosted Response (Overall Study)	0	0		
Treatment-Emergent Response (Overall Study)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with at least one Treatment-Emergent Adverse Event (TEAE)

End point title	Number of subjects with at least one Treatment-Emergent Adverse Event (TEAE)

End point description:

Double-blind Safety Analysis Set: Randomized population who received at least 1 dose or part of a dose of double-blind study drug; Single-blind Safety Analysis Set (SBTP): Randomized population who received at least 1 dose or part of a dose of single-blind study drug.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	35	32
Units: Subjects				
number (not applicable)	11	13	25	25

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with at least one Serious Adverse Event (SAE)

End point title	Number of subjects with at least one Serious Adverse Event (SAE)

End point description:

Double-blind Safety Analysis Set: Randomized population who received at least 1 dose or part of a dose of double-blind study drug; Single-blind Safety Analysis Set: Randomized population who received at least 1 dose or part of a dose of single-blind study drug.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	35	32
Units: Subjects				
number (not applicable)	3	4	4	11

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with liver function laboratory abnormalities

End point title	Number of subjects with liver function laboratory abnormalities

End point description:

Number of subjects with treatment-emergent potentially clinically significant variables (PCSV) during the treatment-emergent adverse event (TEAE) period reported; Double-blind safety analysis set (SAF): Randomized population who received at least 1 dose or part of a dose of double-blind study drug. Subjects analyzed according to treatment received (placebo or evinacumab); Single-Blind SAF: Randomized population who received at least 1 dose or part of a dose of single-blind study drug (SBTP); [Alanine aminotransferase (ALT); Aspartate aminotransferase (AST); Baseline (BL); Upper limit of normal (ULN)]

End point type	Secondary
End point timeframe:	
Up to 48 weeks	

End point values	DB Placebo IV Q4W/SB Evinacumab	DB Placebo/SB Evinacumab IV 15mg/kg Q4W	DB Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Evinacumab/SB Evinacumab IV 15mg/kg Q4W
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	35	32
Units: Subjects				
number (not applicable)				
ALT >2 ULN and <=3 ULN and <=2 ULN at baseline	0	0	1	0
ALT >3 ULN and <=5 ULN and <=3 ULN at BL	0	0	2	0
ALT >5 ULN and <=10 ULN and <=5 ULN at BL	0	1	0	1
ALT 10 ULN and <=20 ULN and <=10 ULN at BL	0	0	0	0
ALT >20 ULN and <=20 ULN at BL	0	0	0	0
AST >2 ULN and <=3 ULN and <=2 ULN at BL	0	0	2	0
AST >3 ULN and <=5 ULN and <=3 ULN at BL	0	1	1	0
AST >5 ULN and <=10 ULN and <=5 ULN at BL	0	0	0	1
AST >10 ULN and <=20 ULN and <=10 ULN at BL	0	0	0	0
AST >20 ULN and <=20 ULN at BL	0	0	0	0
Bilirubin >1.5 ULN - <=2 ULN and =<1.5 ULN at BL	0	0	0	0
Bilirubin >2 ULN and =< 2.0 ULN at BL	0	0	0	0
Alkaline Phosphatase >1.5 ULN and =< 1.5 ULN at BL	0	0	0	2
(ALT>3ULN&TB>2ULN)&(ALT<=3ULN or TB<=2ULN) at BL	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Day 1 up to Last Single-Blind (SB) dose + 168 days (24 weeks)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	DBTP Placebo IV Q4W/SB Evinacumab
Reporting group description:	
Subjects received placebo matching evinacumab intravenously (IV) every 4 weeks (Q4W) on days 1, 29, and 57 during the 12-week double-blind treatment period (DBTP). During the 12-week single-blind treatment period (SBTP), subjects received evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Reporting group title	DBTP Evinacumab IV 15mg/kg Q4W/SB Evinacumab
Reporting group description:	
Subjects received evinacumab 15 mg/kg IV Q4W on days 1, 29, and 57 during the 12-week DBTP. During the 12-week SBTP, subjects continued to receive evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Reporting group title	DB Placebo/SBTP Evinacumab IV 15mg/kg Q4W
Reporting group description:	
Subjects received placebo matching evinacumab intravenously (IV) every 4 weeks (Q4W) on days 1, 29, and 57 during the 12-week double-blind treatment period (DBTP). During the 12-week single-blind treatment period (SBTP), subjects received evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	
Reporting group title	DB Evinacumab/SBTP Evinacumab IV 15mg/kg Q4W
Reporting group description:	
Subjects received evinacumab 15 mg/kg IV Q4W on days 1, 29, and 57 during the 12-week DBTP. During the 12-week SBTP, subjects continued to receive evinacumab 15 mg/kg IV Q4W on days 85, 113, and 141.	

Serious adverse events	DBTP Placebo IV Q4W/SB Evinacumab	DBTP Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Placebo/SBTP Evinacumab IV 15mg/kg Q4W
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)	4 / 35 (11.43%)	4 / 15 (26.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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			
Ischaemic stroke			

subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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			
Pancreatitis acute			
subjects affected / exposed	2 / 16 (12.50%)	3 / 35 (8.57%)	4 / 15 (26.67%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	0 / 15 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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			
Acute respiratory failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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			
Clostridium difficile infection			

subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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
Viral infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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
Metabolic acidosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (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/SBTP Evinacumab IV 15mg/kg Q4W		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 32 (34.38%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Pancreatitis acute				
subjects affected / exposed	8 / 32 (25.00%)			
occurrences causally related to treatment / all	0 / 14			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Liver injury				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Clostridium difficile infection				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral infection				

subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	1 / 32 (3.13%)		
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	DBTP Placebo IV Q4W/SB Evinacumab	DBTP Evinacumab IV 15mg/kg Q4W/SB Evinacumab	DB Placebo/SBTP Evinacumab IV 15mg/kg Q4W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 16 (68.75%)	20 / 35 (57.14%)	13 / 15 (86.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	1 / 15 (6.67%)
occurrences (all)	1	1	1
Vessel puncture site pain			

subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 35 (2.86%)	1 / 15 (6.67%)
occurrences (all)	0	1	2
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	2 / 15 (13.33%)
occurrences (all)	0	2	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	2 / 15 (13.33%)
occurrences (all)	0	2	2
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Blood magnesium decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	2	0	3
Contusion			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 16 (12.50%)	4 / 35 (11.43%)	2 / 15 (13.33%)
occurrences (all)	2	6	3
Migraine			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	1 / 16 (6.25%)	4 / 35 (11.43%)	2 / 15 (13.33%)
occurrences (all)	1	4	2
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	2 / 15 (13.33%)
occurrences (all)	1	1	4
Nausea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
Abdominal distension			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	1 / 35 (2.86%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Diverticulum			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Enteritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Eructation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Food poisoning			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Oesophagitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Pancreatic failure			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Abdominal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	0 / 15 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	0 / 16 (0.00%)	3 / 35 (8.57%)	0 / 15 (0.00%)
occurrences (all)	0	4	0
Pancreatitis acute			
subjects affected / exposed	0 / 16 (0.00%)	1 / 35 (2.86%)	0 / 15 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Azotaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Renal cyst			

subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Renal impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Nodal osteoarthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	0 / 15 (0.00%)
occurrences (all)	0	4	0
Muscle spasms			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 16 (6.25%)	2 / 35 (5.71%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	1	0	1
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Clostridium difficile infection			

subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	2
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	0 / 15 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis viral			
subjects affected / exposed	1 / 16 (6.25%)	0 / 35 (0.00%)	0 / 15 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Influenza			
subjects affected / exposed	0 / 16 (0.00%)	1 / 35 (2.86%)	1 / 15 (6.67%)
occurrences (all)	0	1	1
Laryngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 35 (5.71%)	1 / 15 (6.67%)
occurrences (all)	0	2	1
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 16 (6.25%)	1 / 35 (2.86%)	2 / 15 (13.33%)
occurrences (all)	1	1	2
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 16 (6.25%)	2 / 35 (5.71%)	1 / 15 (6.67%)
occurrences (all)	1	2	1
Hypocalcaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1
Metabolic acidosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 35 (0.00%)	1 / 15 (6.67%)
occurrences (all)	0	0	1

Non-serious adverse events	DB Evinacumab/SBTP Evinacumab IV 15mg/kg Q4W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 32 (68.75%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Vessel puncture site pain			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Hiccups			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		

Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Psychiatric disorders Delirium subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	 0 / 32 (0.00%) 0 1 / 32 (3.13%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all) Blood magnesium decreased subjects affected / exposed occurrences (all)	 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 2 / 32 (6.25%) 2		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) Contusion subjects affected / exposed occurrences (all)	 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0		
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	 0 / 32 (0.00%) 0		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Migraine subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Sciatica subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Dizziness subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	4 / 32 (12.50%) 6		
Diarrhoea subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Abdominal distension subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Abdominal pain upper subjects affected / exposed occurrences (all)	3 / 32 (9.38%) 4		
Diverticulum			

subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Dyspepsia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Enteritis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Eructation				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Food poisoning				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences (all)	1			
Oesophagitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Pancreatic failure				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences (all)	0			
Vomiting				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			
Abdominal discomfort				
subjects affected / exposed	2 / 32 (6.25%)			
occurrences (all)	2			
Constipation				

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Pancreatitis acute			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Azotaemia			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Renal cyst			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Renal impairment			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Nodal osteoarthritis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Back pain			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	5		
Bronchitis			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Clostridium difficile infection			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Laryngitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		

Oral candidiasis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0 0 / 32 (0.00%) 0		
Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all) Type 2 diabetes mellitus subjects affected / exposed occurrences (all) Hypocalcaemia subjects affected / exposed occurrences (all) Metabolic acidosis subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2017	Increased sample size and number of sites; Changed classification of study from phase 1b to phase 2; Added to rationale; Modified inclusion/exclusion criteria; Clarified description of cohorts; Updated enrollment procedure; Updated language regarding study drug concentration and anti-drug antibody concentration; Modified Schedule of Events, Prohibited Medications, Permitted Medications and Procedures; Clarified primary efficacy analysis; Updated contraception language; Added study drug discontinuation and early termination details; Added sites will provide urine pregnancy tests to female patients of childbearing potential to be used at home; Added pregnancy reporting for female partners of male patients; Added an Independent Data Monitoring Committee
31 July 2017	Clarified the age range of the patient population; Modified Schedule of Events; Clarified blinding of lipid measurements and analysis sets
20 September 2017	Updated ADA variables; Modified a secondary objective/endpoint; Allowed more flexibility for a planned interim analysis; Allowed other select individuals at the sponsor to have access to unblinded data for safety or other data review; Modified Schedule of Events; Expanded list of Adverse Events of Special Interest (AESIs) for evinacumab
18 January 2018	Updated descriptions of the cohorts; Updated text regarding blinding for drug product and placebo
15 October 2019	Amended to require consistent use of a condom for all sexually active males in response to recent nonclinical findings in the rabbit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported