Clinical trial results:
A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate Safety and Efficacy of Evolocumab (AMG 145) in Combination With Statin Therapy in Diabetic Subjects With Hyperlipidemia or Mixed Dyslipidemia (BERSON)

Summary

EudraCT number	2013-000723-14
Trial protocol	FR
Global end of trial date	06 December 2017

Results information

Result version number	v1 (current)
This version publication date	19 December 2018
First version publication date	19 December 2018

Trial information

Trial identification

Sponsor protocol code	20120119

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02662569
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	06 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the effect of 12 weeks of subcutaneous evolocumab in combination with daily oral atorvastatin, compared with placebo and daily atorvastatin, on percent change from baseline in low-density lipoprotein cholesterol (LDL-C) in diabetic subjects with hyperlipidemia or mixed dyslipidemia.

Protection of trial subjects:

This study was conducted in accordance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations and guidelines.
The study and all amendments were reviewed by an Independent Ethics Committee (IEC) or Institutional Review Board (IRB) at each center.
The investigator or his/her designee informed the subject of all aspects pertaining to the subject's participation in the study before any screening procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 April 2016
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	China: 453
Country: Number of subjects enrolled	Korea, Republic of: 38
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Russian Federation: 227
Country: Number of subjects enrolled	Turkey: 31
Country: Number of subjects enrolled	Argentina: 58
Country: Number of subjects enrolled	Brazil: 112
Country: Number of subjects enrolled	Colombia: 25
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	United States: 33
Worldwide total number of subjects	986
EEA total number of subjects	3

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)	620
From 65 to 84 years	366
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 102 study centers and randomized at 98 centers in Argentina, Brazil, Canada, China, Colombia, France, Republic of Korea, Russian Federation, Turkey, and the United States from 14 April 2016 to 28 July 2017.

Pre-assignment

Screening details:

After undergoing screening procedures, including laboratory assessments and a screening placebo injection, participants meeting eligibility criteria and completing at least 4 weeks of lipid stabilization on atorvastatin 20 mg daily were randomized in a 1:1:2:2 ratio. Randomization was stratified by entry statin therapy and geographic region.

Period 1

Period 1 title	Overall Study (overall period)
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	Placebo Q2W

Arm description:

Participants received placebo subcutaneous injection once every 2 weeks (Q2W) and 20 mg atorvastatin orally once a day for up to 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo to evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered subcutaneously once every 2 weeks

Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	
Other name	Lipitor
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day

Arm title	Placebo QM

Arm description:

Participants received placebo subcutaneous injection once a month (QM) and 20 mg atorvastatin orally once a day for up to 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo to evolocumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:	
Administered subcutaneously once every month	
Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	
Other name	Lipitor
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Administered orally once a day	
Arm title	Evolocumab Q2W
Arm description:	
Participants received 140 mg evolocumab by subcutaneous injection once every 2 weeks and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	
Other name	Lipitor
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Administered orally once a day	
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details:	
Administered subcutaneously once every 2 weeks	
Arm title	Evolocumab QM
Arm description:	
Participants received 420 mg evolocumab by subcutaneous injection once a month and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Arm type	Experimental
Investigational medicinal product name	Atorvastatin
Investigational medicinal product code	
Other name	Lipitor
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Administered orally once a day	
Investigational medicinal product name	Evolocumab
Investigational medicinal product code	AMG 145
Other name	Repatha
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details:	
Administered subcutaneously once every month	

Number of subjects in period 1	Placebo Q2W	Placebo QM	Evolocumab Q2W
Started	166	161	327
Received Study Drug	164	160	325
Completed	159	160	321
Not completed	7	1	6
Consent withdrawn by subject	6	1	6
Lost to follow-up	1	-	-

Number of subjects in period 1	Evolocumab QM
Started	332
Received Study Drug	332
Completed	328
Not completed	4
Consent withdrawn by subject	4
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Q2W
Reporting group description:	
Participants received placebo subcutaneous injection once every 2 weeks (Q2W) and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Placebo QM
Reporting group description:	
Participants received placebo subcutaneous injection once a month (QM) and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Evolocumab Q2W
Reporting group description:	
Participants received 140 mg evolocumab by subcutaneous injection once every 2 weeks and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Evolocumab QM
Reporting group description:	
Participants received 420 mg evolocumab by subcutaneous injection once a month and 20 mg atorvastatin orally once a day for up to 12 weeks.	

Reporting group values	Placebo Q2W	Placebo QM	Evolocumab Q2W
Number of subjects	166	161	327
Age, Customized Units: Subjects			
18 - 64 years	105	101	206
65 - 84 years	61	60	121
Age Continuous Units: years			
arithmetic mean	61.6	61.0	61.0
standard deviation	± 8.8	± 8.8	± 8.5
Sex: Female, Male Units: Subjects			
Female	102	94	178
Male	64	67	149
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	82	80	164
Black or African American	7	6	11
Native Hawaiian or Other Pacific Islander	0	0	0
White	72	68	140
Multiple	5	6	11
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	29	34	65
Not Hispanic or Latino	137	127	262
Unknown or Not Reported	0	0	0
Stratification Factor: Statin Therapy at Study Entry			
Intensive: at least one of the following recorded for the last 4 weeks prior to screening: atorvastatin ≥			

40 mg once daily (QD); rosuvastatin ≥ 20 mg QD; simvastatin ≥ 80 mg QD; any statin (atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin) QD plus ezetimibe. Non-intensive: Subject has been taking any dose of a statin at least weekly for the last 4 weeks prior to screening and is not included in the intensive statin usage. No statin: Subject is not included in the intensive statin usage or non-intensive statin usage.			
Units: Subjects			
Intensive statin usage	16	15	31
Non-intensive statin usage	83	80	167
No statin	67	66	129
Stratification Factor: Geographic Region Units: Subjects			
China	76	75	150
South Korea	6	5	14
Other countries	84	81	163
Low-density Lipoprotein Cholesterol (LDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	92.2	91.0	92.4
standard deviation	± 32.0	± 30.7	± 33.8
Non-high-density Lipoprotein Cholesterol (non-HDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	119.2	119.4	121.3
standard deviation	± 38.2	± 36.0	± 38.1
Apolipoprotein B100 Concentration			
Apolipoprotein B100 is the primary apolipoprotein of low-density lipoprotein cholesterol particles, and plays a role in moving cholesterol around the body. Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), and with available baseline data, 162, 158, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	82.1	83.4	84.8
standard deviation	± 23.1	± 22.3	± 23.0
Total Cholesterol			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	166.5	169.3	167.8
standard deviation	± 38.6	± 37.5	± 38.9
Total Cholesterol/High-density Lipoprotein Cholesterol(HDL-C) Ratio			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: ratio			
arithmetic mean	3.717	3.598	3.804
standard deviation	± 1.337	± 1.071	± 1.273
Apolipoprotein B100/Apolipoprotein A1 Ratio			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), and with available baseline data,			

162, 158, 325, and 332 subjects in each treatment group respectively.			
Units: ratio			
arithmetic mean	0.573	0.563	0.601
standard deviation	± 0.192	± 0.161	± 0.200
Lipoprotein(a)			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: nmol/L			
arithmetic mean	67.0	71.8	65.6
standard deviation	± 90.9	± 96.5	± 92.5
Triglycerides Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	137.3	150.6	145.9
standard deviation	± 77.3	± 154.6	± 67.5
High-density Lipoprotein Cholesterol (HDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	47.3	49.9	46.5
standard deviation	± 11.9	± 15.2	± 11.5
Very Low-density Lipoprotein Cholesterol (VLDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	27.3	28.4	28.7
standard deviation	± 14.9	± 16.2	± 12.6

Reporting group values	Evolocumab QM	Total	
Number of subjects	332	986	
Age, Customized			
Units: Subjects			
18 - 64 years	208	620	
65 - 84 years	124	366	
Age Continuous			
Units: years			
arithmetic mean	61.6		
standard deviation	± 8.4	-	
Sex: Female, Male			
Units: Subjects			
Female	190	564	
Male	142	422	
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	0	2	
Asian	166	492	
Black or African American	18	42	

Native Hawaiian or Other Pacific Islander	0	0	
White	140	420	
Multiple	8	30	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	67	195	
Not Hispanic or Latino	265	791	
Unknown or Not Reported	0	0	
Stratification Factor: Statin Therapy at Study Entry			
Intensive: at least one of the following recorded for the last 4 weeks prior to screening: atorvastatin ≥ 40 mg once daily (QD); rosuvastatin ≥ 20 mg QD; simvastatin ≥ 80 mg QD; any statin (atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin) QD plus ezetimibe. Non-intensive: Subject has been taking any dose of a statin at least weekly for the last 4 weeks prior to screening and is not included in the intensive statin usage. No statin: Subject is not included in the intensive statin usage or non-intensive statin usage.			
Units: Subjects			
Intensive statin usage	32	94	
Non-intensive statin usage	166	496	
No statin	134	396	
Stratification Factor: Geographic Region Units: Subjects			
China	152	453	
South Korea	13	38	
Other countries	167	495	
Low-density Lipoprotein Cholesterol (LDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	93.5		
standard deviation	± 33.6	-	
Non-high-density Lipoprotein Cholesterol (non-HDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	121.2		
standard deviation	± 37.0	-	
Apolipoprotein B100 Concentration			
Apolipoprotein B100 is the primary apolipoprotein of low-density lipoprotein cholesterol particles, and plays a role in moving cholesterol around the body. Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), and with available baseline data, 162, 158, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	84.4		
standard deviation	± 21.8	-	
Total Cholesterol			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	168.9		

standard deviation	± 38.9	-	
Total Cholesterol/High-density Lipoprotein Cholesterol(HDL-C) Ratio			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: ratio			
arithmetic mean	3.725		
standard deviation	± 1.201	-	
Apolipoprotein B100/Apolipoprotein A1 Ratio			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), and with available baseline data, 162, 158, 325, and 332 subjects in each treatment group respectively.			
Units: ratio			
arithmetic mean	0.586		
standard deviation	± 0.185	-	
Lipoprotein(a)			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: nmol/L			
arithmetic mean	73.2		
standard deviation	± 95.9	-	
Triglycerides Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	139.7		
standard deviation	± 64.9	-	
High-density Lipoprotein Cholesterol (HDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	47.6		
standard deviation	± 12.3	-	
Very Low-density Lipoprotein Cholesterol (VLDL-C) Concentration			
Data are reported for all participants in the full analysis set, consisting of randomized participants who received at least 1 dose of the study drug (placebo or evolocumab), 164, 160, 325, and 332 subjects in each treatment group respectively.			
Units: mg/dL			
arithmetic mean	27.8		
standard deviation	± 12.7	-	

End points

End points reporting groups

Reporting group title	Placebo Q2W
Reporting group description:	
Participants received placebo subcutaneous injection once every 2 weeks (Q2W) and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Placebo QM
Reporting group description:	
Participants received placebo subcutaneous injection once a month (QM) and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Evolocumab Q2W
Reporting group description:	
Participants received 140 mg evolocumab by subcutaneous injection once every 2 weeks and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Evolocumab QM
Reporting group description:	
Participants received 420 mg evolocumab by subcutaneous injection once a month and 20 mg atorvastatin orally once a day for up to 12 weeks.	

Primary: Percent Change From Baseline in LDL-C at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in LDL-C at the Mean of Weeks 10 and 12
End point description:	
End point type	Primary
End point timeframe:	
Baseline and weeks 10 and 12	

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	4.94 (± 3.48)	0.99 (± 3.31)	-65.35 (± 3.09)	-69.05 (± 2.96)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001 [2]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-70.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-75.43
upper limit	-65.16
Variability estimate	Standard error of the mean
Dispersion value	2.61

Notes:

[1] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[2] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001 [4]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-70.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.67
upper limit	-65.41
Variability estimate	Standard error of the mean
Dispersion value	2.35

Notes:

[3] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[4] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Primary: Percent Change From Baseline in LDL-C at Week 12

End point title	Percent Change From Baseline in LDL-C at Week 12

End point description:

End point type	Primary

End point timeframe:

Baseline and week 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	7.10 (± 3.66)	2.63 (± 3.41)	-64.66 (± 3.20)	-62.30 (± 3.02)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.0001 [6]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-71.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	-77.61
upper limit	-65.93
Variability estimate	Standard error of the mean
Dispersion value	2.97

Notes:

[5] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[6] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.0001 [8]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-64.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-69.97
upper limit	-59.89
Variability estimate	Standard error of the mean
Dispersion value	2.56

Notes:

[7] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[8] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit,

and the interaction of treatment with scheduled visit

Secondary: Change From Baseline in LDL-C at the Mean of Weeks 10 and 12	
End point title	Change From Baseline in LDL-C at the Mean of Weeks 10 and 12
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and weeks 10 and 12	

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: mg/dL				
least squares mean (standard error)	-2.1 (± 4.1)	-8.8 (± 4.0)	-64.6 (± 3.6)	-71.9 (± 3.6)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.0001 [10]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-62.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.2
upper limit	-56.9
Variability estimate	Standard error of the mean
Dispersion value	2.9

Notes:

[9] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[10] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM

Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	< 0.0001 [12]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-63.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68.4
upper limit	-57.8
Variability estimate	Standard error of the mean
Dispersion value	2.7

Notes:

[11] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[12] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Change From Baseline in LDL-C at Week 12

End point title	Change From Baseline in LDL-C at Week 12
End point description:	

End point type	Secondary
End point timeframe:	
Baseline and week 12	

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: mg/dL				
least squares mean (standard error)	-0.3 (± 4.2)	-7.3 (± 4.1)	-63.9 (± 3.7)	-66.1 (± 3.7)

Statistical analyses

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	< 0.0001 [14]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-58.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-64.3
upper limit	-53.3
Variability estimate	Standard error of the mean
Dispersion value	2.8

Notes:

[13] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[14] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	< 0.0001 [16]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-63.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-69.7
upper limit	-57.6
Variability estimate	Standard error of the mean
Dispersion value	3.1

Notes:

[15] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[16] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Secondary: Percent Change From Baseline in Non-HDL-C at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in Non-HDL-C at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	4.33 (± 3.05)	0.33 (± 2.95)	-56.57 (± 2.70)	-59.08 (± 2.63)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	< 0.0001 [18]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-60.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.51
upper limit	-56.29
Variability estimate	Standard error of the mean
Dispersion value	2.35

Notes:

[17] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[18] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0.0001 [20]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-59.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.52
upper limit	-55.29
Variability estimate	Standard error of the mean
Dispersion value	2.09

Notes:

[19] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[20] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Non-HDL-C at Week 12

End point title	Percent Change From Baseline in Non-HDL-C at Week 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and week 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	5.87 (± 3.20)	1.30 (± 3.03)	-55.76 (± 2.79)	-59.92 (± 2.69)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.0001 [22]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-61.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.82
upper limit	-56.45
Variability estimate	Standard error of the mean
Dispersion value	2.64

Notes:

[21] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[22] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	< 0.0001 [24]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-54.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.7
upper limit	-49.74
Variability estimate	Standard error of the mean
Dispersion value	2.28

Notes:

[23] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[24] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Apolipoprotein B100 at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in Apolipoprotein B100 at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	1.97 (± 3.31)	-1.52 (± 2.99)	-54.96 (± 3.07)	-56.37 (± 2.72)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	< 0.0001 [26]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-56.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.93
upper limit	-52.93
Variability estimate	Standard error of the mean
Dispersion value	2.03

Notes:

[25] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[26] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.0001 [28]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-54.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.52
upper limit	-51.18
Variability estimate	Standard error of the mean
Dispersion value	1.87

Notes:

[27] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[28] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Apolipoprotein B100 at Week 12

End point title	Percent Change From Baseline in Apolipoprotein B100 at Week 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and week 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	3.17 (± 3.42)	-0.26 (± 3.03)	-53.90 (± 3.14)	-49.68 (± 2.75)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	< 0.0001 [30]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-57.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61.59
upper limit	-52.54
Variability estimate	Standard error of the mean
Dispersion value	2.3

Notes:

[29] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[30] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	< 0.0001 [32]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-49.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.31
upper limit	-45.53
Variability estimate	Standard error of the mean
Dispersion value	1.98

Notes:

[31] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[32] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Secondary: Percent Change From Baseline in Total Cholesterol at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in Total Cholesterol at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	2.89 (± 2.30)	-0.25 (± 2.18)	-38.64 (± 2.04)	-39.74 (± 1.95)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	< 0.0001 [34]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-41.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.95
upper limit	-38.1
Variability estimate	Standard error of the mean
Dispersion value	1.74

Notes:

[33] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[34] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	< 0.0001 [36]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-39.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.47
upper limit	-36.53
Variability estimate	Standard error of the mean
Dispersion value	1.51

Notes:

[35] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[36] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit,

and the interaction of treatment with scheduled visit

Secondary: Percent Change From Baseline in Total Cholesterol at Week 12	
End point title	Percent Change From Baseline in Total Cholesterol at Week 12
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and week 12	

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	4.40 (± 2.40)	0.67 (± 2.24)	-37.82 (± 2.10)	-35.22 (± 1.99)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	< 0.0001 [38]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-42.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.02
upper limit	-38.42
Variability estimate	Standard error of the mean
Dispersion value	1.93

Notes:

[37] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[38] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM

Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[39]
P-value	< 0.0001 [40]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-35.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39.12
upper limit	-32.67
Variability estimate	Standard error of the mean
Dispersion value	1.64

Notes:

[39] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[40] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Total Cholesterol/HDL-C Ratio at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in Total Cholesterol/HDL-C Ratio at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	3.03 (± 2.38)	-2.03 (± 2.41)	-41.06 (± 2.11)	-45.70 (± 2.17)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[41]
P-value	< 0.0001 [42]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-44.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.64
upper limit	-40.54
Variability estimate	Standard error of the mean
Dispersion value	1.81

Notes:

[41] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[42] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[43]
P-value	< 0.0001 [44]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-43.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.9
upper limit	-40.44
Variability estimate	Standard error of the mean
Dispersion value	1.64

Notes:

[43] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[44] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Total Cholesterol/HDL-C Ratio at Week 12

End point title	Percent Change From Baseline in Total Cholesterol/HDL-C Ratio at Week 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and week 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	3.22 (± 2.49)	-1.22 (± 2.47)	-40.72 (± 2.18)	-41.78 (± 2.21)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	< 0.0001 [46]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-43.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.9
upper limit	-39.97
Variability estimate	Standard error of the mean
Dispersion value	2.02

Notes:

[45] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[46] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	< 0.0001 [48]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-40.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-44.08
upper limit	-37.04
Variability estimate	Standard error of the mean
Dispersion value	1.79

Notes:

[47] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[48] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Secondary: Percent Change From Baseline in Apolipoprotein B100/Apolipoprotein A1 Ratio at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in Apolipoprotein

	B100/Apolipoprotein A1 Ratio at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	2.60 (± 3.30)	-1.02 (± 3.09)	-55.60 (± 3.07)	-57.75 (± 2.82)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[49]
P-value	< 0.0001 [50]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-58.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.15
upper limit	-54.25
Variability estimate	Standard error of the mean
Dispersion value	2.01

Notes:

[49] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[50] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[51]
P-value	< 0.0001 [52]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-56.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	-60.53
upper limit	-52.93
Variability estimate	Standard error of the mean
Dispersion value	1.93

Notes:

[51] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[52] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Apolipoprotein B100/Apolipoprotein A1 Ratio at Week 12

End point title	Percent Change From Baseline in Apolipoprotein B100/Apolipoprotein A1 Ratio at Week 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and week 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	3.23 (± 3.39)	-0.10 (± 3.16)	-54.98 (± 3.12)	-51.80 (± 2.86)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[53]
P-value	< 0.0001 [54]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-58.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.59
upper limit	-53.84
Variability estimate	Standard error of the mean
Dispersion value	2.23

Notes:

[53] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[54] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[55]
P-value	< 0.0001 [56]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-51.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.81
upper limit	-47.59
Variability estimate	Standard error of the mean
Dispersion value	2.09

Notes:

[55] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[56] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percentage of Participants With Mean LDL-C at Weeks 10 and 12 of Less Than 70 mg/dL (1.8 mmol/L)

End point title	Percentage of Participants With Mean LDL-C at Weeks 10 and 12 of Less Than 70 mg/dL (1.8 mmol/L)

End point description:

End point type	Secondary

End point timeframe:

Weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percentage of participants				
number (confidence interval 95%)	21.7 (15.9 to 28.7)	19.4 (13.9 to 26.3)	90.1 (86.2 to 92.9)	91.3 (87.6 to 93.9)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[57]
P-value	< 0.0001 [58]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	68.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	60.4
upper limit	74.8

Notes:

[57] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[58] - Cochran-Mantel Haenszel test stratified by entry statin therapy and geographic region.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[59]
P-value	< 0.0001 [60]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	71.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	64.1
upper limit	77.9

Notes:

[59] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[60] - Cochran-Mantel Haenszel test stratified by entry statin therapy and geographic region.

Secondary: Percentage of Participants With LDL-C Less Than 70 mg/dL (1.8 mmol/L) at Week 12

End point title	Percentage of Participants With LDL-C Less Than 70 mg/dL (1.8 mmol/L) at Week 12

End point description:

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percentage of participants				
number (confidence interval 95%)	20.9 (15.2 to 28.2)	21.3 (15.5 to 28.6)	88.2 (84.0 to 91.4)	90.2 (86.2 to 93.1)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[61]
P-value	< 0.0001 [62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	67.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	58.9
upper limit	73.9

Notes:

[61] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[62] - Cochran-Mantel Haenszel test stratified by entry statin therapy and geographic region.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[63]
P-value	< 0.0001 [64]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Treatment Difference
Point estimate	68.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	60.6
upper limit	75.3

Notes:

[63] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[64] - Cochran-Mantel Haenszel test stratified by entry statin therapy and geographic region.

Secondary: Percent Change From Baseline in Lipoprotein(a) at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in Lipoprotein(a) at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	16.89 (± 17.49)	8.48 (± 9.49)	-38.63 (± 13.67)	-42.29 (± 8.49)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[65]
P-value	< 0.0001 [66]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-55.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-92.64
upper limit	-18.4
Variability estimate	Standard error of the mean
Dispersion value	18.85

Notes:

[65] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[66] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[67]
P-value	< 0.0001 [68]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-50.77

Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.82
upper limit	-37.72
Variability estimate	Standard error of the mean
Dispersion value	6.63

Notes:

[67] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[68] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Lipoprotein(a) at Week 12

End point title	Percent Change From Baseline in Lipoprotein(a) at Week 12
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and week 12	

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	26.53 (± 21.78)	7.47 (± 10.40)	-35.93 (± 16.47)	-37.85 (± 9.02)

Statistical analyses

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[69]
P-value	< 0.0001 [70]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-45.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61.87
upper limit	-28.77
Variability estimate	Standard error of the mean
Dispersion value	8.42

Notes:

[69] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[70] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[71]
P-value	< 0.0001 [72]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-62.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-110.89
upper limit	-14.03
Variability estimate	Standard error of the mean
Dispersion value	24.64

Notes:

[71] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[72] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Triglycerides at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in Triglycerides at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	11.54 (± 5.27)	8.48 (± 4.48)	-6.48 (± 4.70)	-7.15 (± 4.02)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W

Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[73]
P-value	= 0.0002 [74]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-18.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.89
upper limit	-10.14
Variability estimate	Standard error of the mean
Dispersion value	4.01

Notes:

[73] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[74] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[75]
P-value	< 0.0001 [76]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-15.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.69
upper limit	-9.58
Variability estimate	Standard error of the mean
Dispersion value	3.08

Notes:

[75] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[76] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in Triglycerides at Week 12

End point title	Percent Change From Baseline in Triglycerides at Week 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and week 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	10.50 (± 5.36)	8.07 (± 4.57)	-5.91 (± 4.75)	-4.24 (± 4.09)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[77]
P-value	= 0.0002 [78]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-16.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.63
upper limit	-8.19
Variability estimate	Standard error of the mean
Dispersion value	14.18

Notes:

[77] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[78] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[79]
P-value	< 0.0001 [80]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-12.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.76
upper limit	-5.86
Variability estimate	Standard error of the mean
Dispersion value	3.28

Notes:

[79] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[80] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in HDL-C at the Mean of Weeks 10 and 12	
End point title	Percent Change From Baseline in HDL-C at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	1.25 (± 2.19)	5.88 (± 2.11)	7.59 (± 1.99)	13.75 (± 1.90)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[81]
P-value	= 0.0003 [82]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	6.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.36
upper limit	9.33
Variability estimate	Standard error of the mean
Dispersion value	1.52

Notes:

[81] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[82] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM

Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[83]
P-value	< 0.0001 [84]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	7.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.1
upper limit	10.65
Variability estimate	Standard error of the mean
Dispersion value	1.41

Notes:

[83] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[84] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in HDL-C at Week 12

End point title	Percent Change From Baseline in HDL-C at Week 12
End point description:	
End point type	Secondary
End point timeframe:	
Baseline and week 12	

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	2.57 (± 2.29)	6.04 (± 2.18)	8.45 (± 2.04)	14.18 (± 1.95)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[85]
P-value	= 0.0003 [86]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	5.88

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.49
upper limit	9.27
Variability estimate	Standard error of the mean
Dispersion value	1.72

Notes:

[85] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[86] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[87]
P-value	< 0.0001 [88]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	8.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.03
upper limit	11.25
Variability estimate	Standard error of the mean
Dispersion value	1.58

Notes:

[87] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[88] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Secondary: Percent Change From Baseline in VLDL-C at the Mean of Weeks 10 and 12

End point title	Percent Change From Baseline in VLDL-C at the Mean of Weeks 10 and 12

End point description:

End point type	Secondary

End point timeframe:

Baseline and weeks 10 and 12

End point values	Placebo Q2W	Placebo QM	Evolocumab Q2W	Evolocumab QM
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	164	160	325	332
Units: percent change				
least squares mean (standard error)	9.63 (± 4.70)	7.92 (± 4.43)	-17.55 (± 4.19)	-16.09 (± 3.99)

Statistical analyses

Statistical analysis title	Evolocumab Q2W vs Placebo Q2W
Comparison groups	Placebo Q2W v Evolocumab Q2W
Number of subjects included in analysis	489
Analysis specification	Pre-specified
Analysis type	superiority[89]
P-value	< 0.0001 [90]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-27.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.2
upper limit	-20.17
Variability estimate	Standard error of the mean
Dispersion value	3.57

Notes:

[89] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[90] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit

Statistical analysis title	Evolocumab QM vs Placebo QM
Comparison groups	Placebo QM v Evolocumab QM
Number of subjects included in analysis	492
Analysis specification	Pre-specified
Analysis type	superiority[91]
P-value	< 0.0001 [92]
Method	Repeated measures linear effects model
Parameter estimate	LS Mean Treatment Difference
Point estimate	-24.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.88
upper limit	-18.14
Variability estimate	Standard error of the mean
Dispersion value	2.99

Notes:

[91] - Multiplicity adjusted p-value is significant if less than the familywise error rate of 0.05.

[92] - The model includes treatment group, entry statin therapy and geographic region, scheduled visit, and the interaction of treatment with scheduled visit.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first dose of study drug (evolocumab or placebo) to 30 days after the last dose; up to 14 weeks.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Placebo Q2W
Reporting group description:	
Participants received placebo subcutaneous injection once every 2 weeks (Q2W) and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Evolocumab Q2W
Reporting group description:	
Participants received 140 mg evolocumab by subcutaneous injection once every 2 weeks and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Evolocumab QM
Reporting group description:	
Participants received 420 mg evolocumab by subcutaneous injection once a month and 20 mg atorvastatin orally once a day for up to 12 weeks.	
Reporting group title	Placebo QM
Reporting group description:	
Participants received placebo subcutaneous injection once a month (QM) and 20 mg atorvastatin orally once a day for up to 12 weeks.	

Serious adverse events	Placebo Q2W	Evolocumab Q2W	Evolocumab QM
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 164 (3.66%)	10 / 325 (3.08%)	22 / 332 (6.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	0 / 332 (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			
Arteriosclerosis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypertension			
subjects affected / exposed	1 / 164 (0.61%)	0 / 325 (0.00%)	0 / 332 (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
Hypertensive crisis			
subjects affected / exposed	1 / 164 (0.61%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral venous disease			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
General disorders and administration site conditions			
Cyst			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
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 disorders			
Acute coronary syndrome			

subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
Angina pectoris			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
Atrial fibrillation			
subjects affected / exposed	2 / 164 (1.22%)	0 / 325 (0.00%)	2 / 332 (0.60%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
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 / 164 (0.00%)	0 / 325 (0.00%)	0 / 332 (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
Carpal tunnel syndrome			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
Cerebral infarction			
subjects affected / exposed	0 / 164 (0.00%)	2 / 325 (0.62%)	0 / 332 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			

subjects affected / exposed	1 / 164 (0.61%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	0 / 332 (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
Lacunar stroke			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular encephalopathy			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
Gastric ulcer			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
Small intestinal obstruction			

subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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			
Nephropathy			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
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			
Back pain			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Herpes zoster cutaneous disseminated			
subjects affected / exposed	1 / 164 (0.61%)	0 / 325 (0.00%)	0 / 332 (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
Lung infection			

subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	0 / 332 (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
Periodontitis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
Tonsillitis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	0 / 332 (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
Urinary tract infection			
subjects affected / exposed	0 / 164 (0.00%)	1 / 325 (0.31%)	1 / 332 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	0 / 332 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 164 (0.00%)	0 / 325 (0.00%)	3 / 332 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo QM		

Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 160 (3.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma gastric			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteriosclerosis			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral venous disease			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Cyst			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			

subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 160 (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 / 160 (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	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Carpal tunnel syndrome			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic neuropathy			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lacunar stroke			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular encephalopathy			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastric ulcer			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephropathy			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myalgia			

subjects affected / exposed	0 / 160 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rheumatoid arthritis				
subjects affected / exposed	0 / 160 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Herpes zoster cutaneous disseminated				
subjects affected / exposed	0 / 160 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 160 (0.63%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periodontitis				
subjects affected / exposed	0 / 160 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 160 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 160 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 160 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 160 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo Q2W	Evolocumab Q2W	Evolocumab QM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 164 (17.07%)	45 / 325 (13.85%)	49 / 332 (14.76%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 164 (3.66%)	8 / 325 (2.46%)	5 / 332 (1.51%)
occurrences (all)	6	8	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 164 (2.44%)	1 / 325 (0.31%)	6 / 332 (1.81%)
occurrences (all)	4	1	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 164 (0.61%)	3 / 325 (0.92%)	3 / 332 (0.90%)
occurrences (all)	1	8	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 164 (3.66%)	9 / 325 (2.77%)	11 / 332 (3.31%)
occurrences (all)	8	9	13
Upper respiratory tract infection			

subjects affected / exposed	6 / 164 (3.66%)	9 / 325 (2.77%)	13 / 332 (3.92%)
occurrences (all)	8	9	13
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 164 (1.22%)	15 / 325 (4.62%)	15 / 332 (4.52%)
occurrences (all)	2	15	15
Hypoglycaemia			
subjects affected / exposed	5 / 164 (3.05%)	2 / 325 (0.62%)	2 / 332 (0.60%)
occurrences (all)	5	2	2

Non-serious adverse events	Placebo QM		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 160 (13.75%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 160 (1.88%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 160 (1.25%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 160 (2.50%)		
occurrences (all)	4		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 160 (3.75%)		
occurrences (all)	7		
Upper respiratory tract infection			
subjects affected / exposed	5 / 160 (3.13%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	4 / 160 (2.50%)		
occurrences (all)	4		
Hypoglycaemia			

subjects affected / exposed occurrences (all)	0 / 160 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2013	• added MMTT with 1 time point for all subjects • replaced "AMG 145" with "evolocumab" throughout the protocol • updated the contraception language
29 July 2015	Steroid analyte testing was added for Chinese subjects, following a request from China Food and Drug Administration to include this as part of the study, since steroid hormones are synthesized from cholesterol precursors, theoretically very low circulating cholesterol could be associated with steroid hormone deficiency.
11 November 2015	• removed potential endpoint adjudication by a clinical events committee • added/updated safety language on the reporting of adverse device effects to include assessment of such events for subjects on Q2W investigational product during the end-of-study contact (eg, phone call) at week 14 and clarify assessment of these events throughout the study • clarified use of effective birth control • clarified definition of product complaint • updated pregnancy and lactation reporting procedures

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported