



Clinical trial results:

A phase IIIb, efficacy, and safety study of rosuvastatin in children and adolescents 10 to 17 years of age with heterozygous familial hypercholesterolemia (HeFH): a 12-week, double-blind, randomized, multi-center, placebo-controlled study with a 40-week, open-label, follow-up period.

Summary

EudraCT number	2006-002616-96
Trial protocol	NL ES Outside EU/EEA
Global end of trial date	04 June 2008

Results information

Result version number	v1 (current)
This version publication date	16 April 2016
First version publication date	16 April 2016

Trial information

Trial identification

Sponsor protocol code	D3561C00087
-----------------------	-------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00355615
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Pepparedsleden 1, Mölndal, Sweden, SE-431 83
Public contact	Robin Mukherjee, R&D/GMD/Biometrics & Information Sciences, AZTrial_Results_Posting@astrazeneca.com
Scientific contact	Robin Mukherjee, R&D/GMD/Biometrics & Information Sciences, AZTrial_Results_Posting@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000022-PIP01-07
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	09 March 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 June 2008
Global end of trial reached?	Yes
Global end of trial date	04 June 2008
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 determine the efficacy of once-daily rosuvastatin in reducing LDL C in children and adolescents aged 10-17 years with HeFH from baseline to the end of the 12 week, double-blind treatment period.

Protection of trial subjects:

An independent Safety Committee monitored blinded data for safety issues during the course of the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 July 2006
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	United States: 17
Country: Number of subjects enrolled	Canada: 65
Country: Number of subjects enrolled	Netherlands: 96
Country: Number of subjects enrolled	Norway: 29
Country: Number of subjects enrolled	Spain: 15
Worldwide total number of subjects	222
EEA total number of subjects	140

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)	48
Adolescents (12-17 years)	174
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

One-hundred male and female (Tanner stages II to V, at least 1 year post-menarche) children and adolescents (aged 10 to 17 years with Heterozygous familial hypercholesterolemia) were randomized into the study, from 20 sites located in The United States (3 sites), The Netherlands (7 sites), Norway (1 site), Spain (3 sites), and Canada (6 sites).

Pre-assignment

Screening details:

Patients entered a 6 week dietary lead-in/drug washout period. Eligible patients were then randomly assigned to double-blind treatment with rosuvastatin 5 mg, 10 mg, 20 mg, or matching placebo, administered orally once daily for 12 weeks.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	rosuva 5

Arm description:

rosuvastatin 5 mg

Arm type	Experimental
Investigational medicinal product name	CRESTOR Rosuvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5mg

Arm title	rosuva 10
------------------	-----------

Arm description:

rosuvastatin 10 mg

Arm type	Experimental
Investigational medicinal product name	CRESTOR Rosuvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10mg

Arm title	rosuva 20
------------------	-----------

Arm description:

rosuvastatin 20 mg

Arm type	Experimental
----------	--------------

Investigational medicinal product name	CRESTOR Rosuvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20mg

Arm title	placebo
------------------	---------

Arm description:

placebo

Arm type	Placebo
Investigational medicinal product name	PLACEBO
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

NA

Number of subjects in period 1^[1]	rosuva 5	rosuva 10	rosuva 20
Started	42	44	45
Completed	41	43	44
Not completed	1	1	1
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	1	-	-
Protocol deviation	-	-	1

Number of subjects in period 1^[1]	placebo
Started	46
Completed	45
Not completed	1
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Protocol deviation	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects reported in the baseline period is not the same as the number enrolled as the week 0 baseline visit (#3) is preceded by two visits at weeks -6 and -1.

Period 2

Period 2 title	40-week rosuvastatin open label period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	rosuva ol
------------------	-----------

Arm description:

rosuvastatin open label

Arm type	Experimental
Investigational medicinal product name	CRESTOR Rosuvastatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg

Number of subjects in period 2	rosuva ol
Started	173
Completed	164
Not completed	9
Consent withdrawn by subject	3
Adverse event, non-fatal	4
investigational site closed	1
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	rosuva 5
Reporting group description:	rosuvastatin 5 mg
Reporting group title	rosuva 10
Reporting group description:	rosuvastatin 10 mg
Reporting group title	rosuva 20
Reporting group description:	rosuvastatin 20 mg
Reporting group title	placebo
Reporting group description:	placebo

Reporting group values	rosuva 5	rosuva 10	rosuva 20
Number of subjects	42	44	45
Age categorical Units: Subjects			
Children (2-11 years)	2	0	0
Adolescents (12-17 years)	40	44	45
Age Continuous Units: years			
arithmetic mean	14.3	14.6	14.4
full range (min-max)	10 to 17	11 to 18	11 to 18
Gender, Male/Female Units: Participants			
Female	26	25	22
Male	16	19	23

Reporting group values	placebo	Total	
Number of subjects	46	177	
Age categorical Units: Subjects			
Children (2-11 years)	1	3	
Adolescents (12-17 years)	45	174	
Age Continuous Units: years			
arithmetic mean	14.4		
full range (min-max)	10 to 17	-	
Gender, Male/Female Units: Participants			
Female	24	97	
Male	22	80	

End points

End points reporting groups

Reporting group title	rosuva 5
Reporting group description:	rosuvastatin 5 mg
Reporting group title	rosuva 10
Reporting group description:	rosuvastatin 10 mg
Reporting group title	rosuva 20
Reporting group description:	rosuvastatin 20 mg
Reporting group title	placebo
Reporting group description:	placebo
Reporting group title	rosuva ol
Reporting group description:	rosuvastatin open label

Primary: Percent change in low-density lipoprotein cholesterol (LDL-C) from baseline (Day 0) to the end of the 12-week double-blind treatment phase

End point title	Percent change in low-density lipoprotein cholesterol (LDL-C) from baseline (Day 0) to the end of the 12-week double-blind treatment phase
End point description:	Percent change in low-density lipoprotein cholesterol (LDL-C) = (final value - Baseline value)/Baseline value * 100
End point type	Primary
End point timeframe:	12 weeks

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: percentage				
arithmetic mean (standard deviation)	-38.5 (± 11.38)	-44.4 (± 12.15)	-50.2 (± 13.3)	-0.5 (± 13.18)

Statistical analyses

Statistical analysis title	Change from randomization to Week 12 in LDL-C
Statistical analysis description:	Analysis of Covariance (ANCOVA) with the baseline LDL-C as a covariate and including treatment as a fixed effect.
Comparison groups	rosuva 5 v placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-37.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.8
upper limit	-32.3
Variability estimate	Standard deviation

Notes:

[1] - Rosuvastatin difference vs placebo

Statistical analysis title	Change from randomization to week 12 in LDL-C
Statistical analysis description:	
Analysis of Covariance (ANCOVA) with the baseline LDL-C as covariate and including treatment as fixed effect.	
Comparison groups	rosuva 10 v placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-44.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.1
upper limit	-38.8
Variability estimate	Standard deviation

Statistical analysis title	Change from randomization to Week 12 in LDL-C
Statistical analysis description:	
Analysis of Covariance (ANCOVA) with the baseline LDL-C as a covariate and including treatment as a fixed effect.	
Comparison groups	rosuva 20 v placebo
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-50

Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.4
upper limit	-44.1
Variability estimate	Standard deviation

Secondary: Percent change in LDL-C and other lipid parameters from baseline to Week 6, and at end of double-blind dose treatment phase (Week 12)

End point title	Percent change in LDL-C and other lipid parameters from baseline to Week 6, and at end of double-blind dose treatment phase (Week 12)
End point description: Percent change from baseline in LDL-C after six week of treatment	
End point type	Secondary
End point timeframe: 6 weeks	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: percentage				
arithmetic mean (standard deviation)	-40.3 (± 12.22)	-45.2 (± 11.15)	-50 (± 11.42)	-0.6 (± 13.63)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent control rate based on achievement of LDL-C target of <110 mg/dL during double-blind dose treatment

End point title	Percent control rate based on achievement of LDL-C target of <110 mg/dL during double-blind dose treatment
End point description: Percent of patients achieving LDL-C < 110 mg/dL out of the total patients in each treatment group	
End point type	Secondary
End point timeframe: 12 weeks	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: Percent of Participants				
number (not applicable)	11.9	40.9	40.9	0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in HDL-C

End point title	Percent change in HDL-C
End point description: Percent change in high-density lipoprotein cholesterol (HDL-C) after 12 weeks of treatment	
End point type	Secondary
End point timeframe: After 12 weeks of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: percent change				
arithmetic mean (standard deviation)	4.5 (± 15.53)	10.1 (± 14.19)	8.9 (± 14.11)	7.6 (± 17.89)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Non-HDL-C at 12 weeks

End point title	Percent change in Non-HDL-C at 12 weeks
End point description: Percent change in non-HDL-C at 12 weeks	
End point type	Secondary
End point timeframe: After 12 weeks of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: percent change				
arithmetic mean (standard deviation)	-36.3 (± 9.98)	-42.8 (± 11.5)	-47.7 (± 13.5)	-0.8 (± 11.89)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in triglycerides (TG)

End point title	Percent change in triglycerides (TG)
End point description:	Percent change in tryglycerides (TG) after 12 weeks of treatment
End point type	Secondary
End point timeframe:	After 12 weeks of treatment

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: percent change				
arithmetic mean (standard deviation)	2.6 (± 49.07)	-14.2 (± 29.66)	-7.9 (± 55.88)	3.4 (± 48.27)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in total cholesterol (TC)

End point title	Percent change in total cholesterol (TC)
End point description:	Percent change from baseline in total cholesterol after 12 weeks of treatment
End point type	Secondary
End point timeframe:	After 12 weeks of treatment

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: percent change				
arithmetic mean (standard deviation)	-30 ($\pm$ 9.63)	-34.1 ($\pm$ 9.5)	-38.9 ($\pm$ 12.08)	0.2 ($\pm$ 10.53)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in apolipoprotein A-1 (ApoA-1)

End point title	Percent change in apolipoprotein A-1 (ApoA-1)
End point description: Percent change in ApoA-1 after 12 weeks of treatment	
End point type	Secondary
End point timeframe: After 12 weeks of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	43	43	46
Units: mean percent change				
arithmetic mean (standard deviation)	2.3 ($\pm$ 9.69)	4.3 ($\pm$ 9.85)	3.9 ($\pm$ 10.68)	3.6 ($\pm$ 15.59)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in apolipoprotein B (ApoB)

End point title	Percent change in apolipoprotein B (ApoB)
End point description: Percent change in ApoB after 12 weeks of treatment	
End point type	Secondary
End point timeframe: After 12 weeks of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	43	43	46
Units: mean percent change				
arithmetic mean (standard deviation)	-32.1 (± 9.13)	-37.8 (± 11.75)	-40.7 (± 13.91)	-1.5 (± 14.67)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in ApoB/ApoA-1

End point title	Percent change in ApoB/ApoA-1
End point description: Percent change in the ratio of ApoB/ApoA-1 after 12 weeks of treatment	
End point type	Secondary
End point timeframe: After 12 weeks of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	43	43	46
Units: mean percent change				
arithmetic mean (standard deviation)	-33.1 (± 9.99)	-40 (± 12.06)	-42.8 (± 12.23)	-3.4 (± 16.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in LDL-C/HDL-C

End point title	Percent change in LDL-C/HDL-C
End point description: Percent change in the ratio of LDL-C/HDL-C after 12 weeks of treatment	
End point type	Secondary
End point timeframe: After 12 week of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: mean percent change				
arithmetic mean (standard deviation)	-40.4 (± 11.36)	-48.6 (± 13.26)	-53.6 (± 12.85)	-5.5 (± 17.98)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in TC/HDL-C

End point title	Percent change in TC/HDL-C
End point description: Percent change in the ratio of TC/HDL-C after 12 weeks of treatment	
End point type	Secondary
End point timeframe: After 12 weeks of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: mean percent change				
arithmetic mean (standard deviation)	-32.1 (± 10.72)	-39.3 (± 11.55)	-43.2 (± 11.76)	-5.2 (± 15.03)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in non-HDL-C/HDL-C

End point title	Percent change in non-HDL-C/HDL-C
End point description: Percent change in the ratio of non-HDL-C/HDL-C after 12 weeks of treatment	
End point type	Secondary
End point timeframe: After 12 weeks of treatment	

End point values	rosuva 5	rosuva 10	rosuva 20	placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	44	44	46
Units: mean percent change				
arithmetic mean (standard deviation)	-37.9 (± 12.12)	-47.1 (± 13.12)	-51.2 (± 13.18)	-5.8 (± 17.63)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From dietary lead-in period(week -1) to end of study(Week 52).

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	11.0
--------------------	------

Reporting groups

Reporting group title	rosuva 5
-----------------------	----------

Reporting group description:

rosuvastatin 5 mg

Reporting group title	rosuva 10
-----------------------	-----------

Reporting group description:

rosuvastatin 10 mg

Reporting group title	rosuva 20
-----------------------	-----------

Reporting group description:

rosuvastatin 20 mg

Reporting group title	placebo
-----------------------	---------

Reporting group description:

placebo

Reporting group title	rosuva ol
-----------------------	-----------

Reporting group description:

rosuvastatin open label

Serious adverse events	rosuva 5	rosuva 10	rosuva 20
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 44 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Eye disorders			
Vision Blurred			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 44 (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
Skin and subcutaneous tissue disorders			
Rash Vesicular			
alternative dictionary used: MedDRA 11.0			

subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 44 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	0 / 44 (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	placebo	rosuva ol	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 46 (2.17%)	2 / 173 (1.16%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Eye disorders			
Vision Blurred			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 46 (2.17%)	0 / 173 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash Vesicular			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 46 (0.00%)	1 / 173 (0.58%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 46 (0.00%)	1 / 173 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-serious adverse events	rosuva 5	rosuva 10	rosuva 20
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 42 (28.57%)	14 / 44 (31.82%)	17 / 44 (38.64%)
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	6 / 42 (14.29%)	7 / 44 (15.91%)	9 / 44 (20.45%)
occurrences (all)	6	7	9
General disorders and administration site conditions			
Fatigue			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	1 / 42 (2.38%)	1 / 44 (2.27%)	1 / 44 (2.27%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Nausea			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 42 (4.76%)	0 / 44 (0.00%)	2 / 44 (4.55%)
occurrences (all)	2	0	2
Tonsillitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	3 / 44 (6.82%)
occurrences (all)	0	0	3
Infections and infestations			
Influenza			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	2 / 42 (4.76%)	2 / 44 (4.55%)	0 / 44 (0.00%)
occurrences (all)	2	2	0
Nasopharyngitis			
alternative dictionary used: MedDRA 11.0			
subjects affected / exposed	3 / 42 (7.14%)	7 / 44 (15.91%)	7 / 44 (15.91%)
occurrences (all)	3	7	7

Non-serious adverse events	placebo	rosuva ol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 46 (36.96%)	75 / 173 (43.35%)	

Nervous system disorders Headache alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all)	9 / 46 (19.57%) 9	29 / 173 (16.76%) 29	
General disorders and administration site conditions Fatigue alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all)	0 / 46 (0.00%) 0	9 / 173 (5.20%) 9	
Gastrointestinal disorders Nausea alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all) Tonsillitis alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all)	2 / 46 (4.35%) 2 1 / 46 (2.17%) 1	10 / 173 (5.78%) 10 2 / 173 (1.16%) 2	
Infections and infestations Influenza alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all) Nasopharyngitis alternative dictionary used: MedDRA 11.0 subjects affected / exposed occurrences (all)	4 / 46 (8.70%) 4 5 / 46 (10.87%) 5	14 / 173 (8.09%) 14 36 / 173 (20.81%) 36	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2006	Substudy is no longer a part of the main study
08 December 2006	HeHF definition: Definition expanded to provide guidance for LDL criteria in statin treated relatives
08 December 2006	Removed the text "in a first degree relative" in order to be consistent with the FDA Written.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: