Clinical trial results:
An Efficacy and 2-Year Safety Study of Open-label Rosuvastatin in Children and Adolescents (aged from 6 to less than 18 years) with Familial Hypercholesterolaemia

Summary

EudraCT number	2009-016492-29
Trial protocol	NL BE Outside EU/EEA
Global end of trial date	08 February 2013

Results information

Result version number	v1 (current)
This version publication date	08 May 2016
First version publication date	08 May 2016

Trial information

Trial identification

Sponsor protocol code	D3561C00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01078675
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca, R&D, B&I
Sponsor organisation address	Pepparedsleden 1, Molndal, Sweden, 431 83
Public contact	Robin Mukherjee, GPS, Biometrics and Information Sciences, robin.mukherjee@astrazeneca.com
Scientific contact	Robin Mukherjee, GPS, Biometrics and Information Sciences, robin.mukherjee@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 June 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 February 2013
Global end of trial reached?	Yes
Global end of trial date	08 February 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study were: • To assess the efficacy of rosuvastatin in paediatric patients with FH. • To establish long-term safety, tolerability and efficacy of rosuvastatin in paediatric patients with FH. • To characterise the PK profile of rosuvastatin in paediatric patients, aged from 6 to less than Tanner Stage II, with FH.

Protection of trial subjects:

An external consultant functioned as an independent safety monitor to assess safety data beginning 4 months after the first patient was enrolled into the trial and then approximately every 4 months until study completion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Canada: 114
Country: Number of subjects enrolled	Netherlands: 126
Country: Number of subjects enrolled	Norway: 59
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	327
EEA total number of subjects	194

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)	131

Adolescents (12-17 years)	196
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

250 patients with FH were screened. Additionally, 65 healthy siblings (HS) were enrolled. HS refers to healthy subjects that were siblings of either the study participants or other paediatric patients with HeFH that were not participating in the study. HS were enrolled to have assessments of cIMT, but did not participate further.

Pre-assignment

Screening details:

Statin-naïve patients including all patients aged 6 to <10 years, were qualified for by meeting all inclusion, exclusion and LDL-C criteria at Visit 1. Previously treated patients qualified by meeting all inclusion and exclusion criteria at screening Visits 1 and 2 and by meeting LDL-C criteria at Visit 2.

Period 1

Period 1 title	Visit 3
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Rosuvastatin

Arm description:

Rosuvastatin 5 mg, 10 mg or 20 mg

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

Dosage and administration details:

5 to 20 mg

Arm title	Single Dose PK

Arm description: -

Arm type	Modified Intention to Treat
Investigational medicinal product name	Rosuvastatin, Crestor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg

Arm title	Healthy Siblings

Arm description: -

Arm type	Modified Intention to Treat
Investigational medicinal product name	Control
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
Control

Number of subjects in period 1	Rosuvastatin	Single Dose PK	Healthy Siblings
Started	250	12	65
Completed	250	12	65

Period 2

Period 2 title	Overall Study
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Rosuvastatin

Arm description:
Rosuvastatin 5 mg, 10 mg or 20 mg

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

Dosage and administration details:
5 to 20 mg

Arm title	Single Dose PK

Arm description: -

Arm type	Modified Intention to Treat
Investigational medicinal product name	Rosuvastatin, Crestor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
10 mg

Arm title	Healthy Siblings

Arm description: -	
Arm type	Modified Intention to Treat
Investigational medicinal product name	Control
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Control

Number of subjects in period 2	Rosuvastatin	Single Dose PK	Healthy Siblings
Started	250	12	65
Patients treated	198	12	65
Completed	182	12	65
Not completed	68	0	0
Consent withdrawn by subject	7	-	-
Provided in CRF for specific reasons	2	-	-
Adverse event, non-fatal	3	-	-
Protocol deviation	56	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Rosuvastatin
Reporting group description: Rosuvastatin 5 mg, 10 mg or 20 mg	
Reporting group title	Single Dose PK
Reporting group description: -	
Reporting group title	Healthy Siblings
Reporting group description: -	

Reporting group values	Rosuvastatin	Single Dose PK	Healthy Siblings
Number of subjects	250	12	65
Age categorical Units: Subjects			
6-<10	70	12	21
10-<14	96	0	22
14-<18	84	0	22
Age Continuous | Years Units: Years			
arithmetic mean	11.8	8	11.5
standard deviation	± 3.2	± 0.9	± 3.5
Gender, Male/Female Units: Participants			
Female	127	7	32
Male	123	5	33
Race/Ethnicity, Customized Units: Subjects			
Caucasian	220	12	53
non-Caucasian	30	0	12

Reporting group values	Total		
Number of subjects	327		
Age categorical Units: Subjects			
6-<10	103		
10-<14	118		
14-<18	106		
Age Continuous | Years Units: Years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: Participants			
Female	166		
Male	161		

Race/Ethnicity, Customized Units: Subjects			
Caucasian	285		
non-Caucasian	42		

Subject analysis sets

Subject analysis set title	Healthy Siblings
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Controls to HeFH patients in the cIMT evaluations

Subject analysis set title	Single dose PK
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Rosuvastatin 10 mg

Subject analysis set title	ITT Baseline
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Including patients who took atleast 1 dose of study medication and had a baseline and at least 1 LDL-C measured in a subsequent visit.

Subject analysis set title	ITT 24 month
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Including patients who took atleast 1 dose of study medication and had a baseline and at least 1 LDL-C measured in a subsequent visit.

Reporting group values	Healthy Siblings	Single dose PK	ITT Baseline
Number of subjects	65	12	197
Age categorical Units: Subjects			
6-<10	21	12	63
10-<14	22	0	72
14-<18	22	0	62
Age Continuous | Years Units: Years			
arithmetic mean	11.5	8	11.6
standard deviation	± 3.5	± 0.9	± 3.3
Gender, Male/Female Units: Participants			
Female	32	7	110
Male	33	5	87
Race/Ethnicity, Customized Units: Subjects			
Caucasian	53	12	177
non-Caucasian	12	0	20

Reporting group values	ITT 24 month		
Number of subjects	197		
Age categorical Units: Subjects			
6-<10	63		
10-<14	72		

14-<18	62		

Age Continuous | Years Units: Years			
arithmetic mean	13.6		
standard deviation	± 3.3		
Gender, Male/Female Units: Participants			
Female	110		
Male	87		
Race/Ethnicity, Customized Units: Subjects			
Caucasian	177		
non-Caucasian	20		

End points

End points reporting groups

Reporting group title	Rosuvastatin
Reporting group description: Rosuvastatin 5 mg, 10 mg or 20 mg	
Reporting group title	Single Dose PK
Reporting group description: -	
Reporting group title	Healthy Siblings
Reporting group description: -	
Reporting group title	Rosuvastatin
Reporting group description: Rosuvastatin 5 mg, 10 mg or 20 mg	
Reporting group title	Single Dose PK
Reporting group description: -	
Reporting group title	Healthy Siblings
Reporting group description: -	
Subject analysis set title	Healthy Siblings
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Controls to HeFH patients in the cIMT evaluations	
Subject analysis set title	Single dose PK
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Rosuvastatin 10 mg	
Subject analysis set title	ITT Baseline
Subject analysis set type	Intention-to-treat
Subject analysis set description: Including patients who took atleast 1 dose of study medication and had a baseline and at least 1 LDL-C measured in a subsequent visit.	
Subject analysis set title	ITT 24 month
Subject analysis set type	Intention-to-treat
Subject analysis set description: Including patients who took atleast 1 dose of study medication and had a baseline and at least 1 LDL-C measured in a subsequent visit.	

Primary: Percent Change from Baseline in LDL-C

End point title	Percent Change from Baseline in LDL-C
End point description: Negative values represent a decrease and positive values represent an increase. In total, 198 patients were treated. One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.	
End point type	Primary
End point timeframe: At Month 3, Month 12 and Month 24	

End point values	Rosuvastatin	ITT Baseline	ITT 24 month	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	197	197	197	
Units: Percentage change				
arithmetic mean (standard deviation)				
LDL-C %Change from Baseline at month 3	-37.86 (± 14.392)	0 (± 0)	-37.86 (± 14.392)	
LDL-C %Change from Baseline at month 12	-43.67 (± 14.896)	0 (± 0)	-43.67 (± 14.896)	
LDL-C %Change from Baseline at month 24	-42.88 (± 18.222)	0 (± 0)	-42.88 (± 18.222)	

Statistical analyses

Statistical analysis title	Percent Change from Baseline in LDL Cholesterol
Comparison groups	Rosuvastatin v ITT 24 month v ITT Baseline
Number of subjects included in analysis	591
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	ANCOVA
Parameter estimate	LS Means
Point estimate	-42.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.44
upper limit	-40.32
Variability estimate	Standard deviation
Dispersion value	18.222

Notes:

[1] - The p-value is actually less than 0.001

Secondary: Sexual Maturation by Tanner Staging at baseline

End point title	Sexual Maturation by Tanner Staging at baseline

End point description:

Tanner stages (I-V) was used to characterize physical development in children and adolescent. The stages was based on external primary and secondary sex characteristics, such as the size of the breasts, genitalia, and development of pubic hair. Tanner stage is considered going up when the organs grow bigger.

End point type	Secondary

End point timeframe:

At Baseline

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Participants				
Tanner Stage I at Baseline	81			
Tanner Stage II at Baseline	32			
Tanner Stage III at Baseline	18			
Tanner Stage IV at Baseline	44			
Tanner Stage V at Baseline	21			
Not Recorded at Baseline	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Single Dose PK - Cmax

End point title	Single Dose PK - Cmax

End point description:

Serial plasma samples were taken at baseline (Week 0) at: 0.5 hours pre-dose and at 0.5, 1, 2, 3, 4, 5, 6, 9, 12 hours and on Day 1 at 24 hours after the single 10 mg dosing

End point type	Secondary

End point timeframe:

Serial blood samples over 24 hours.

End point values	Single Dose PK	Single dose PK		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	12	12		
Units: ng/mL				
arithmetic mean (standard deviation)	3.5717 (± 3.2235)	3.5717 (± 3.2235)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in HDL-C, TC, TG, non-HDL-C, LDL-C/HDL-C, TC/HDL-C, non HDL C/HDL-C, ApoB, ApoA-1, and ApoB/ApoA-1

End point title	Percent Change from Baseline in HDL-C, TC, TG, non-HDL-C, LDL-C/HDL-C, TC/HDL-C, non HDL C/HDL-C, ApoB, ApoA-1, and ApoB/ApoA-1

End point description:

One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.

End point type	Secondary

End point timeframe:
At Month 3, Month 12 and Month 24

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Percent change				
arithmetic mean (standard deviation)				
HDL-C %Change from Baseline at Month 3	5.67 (± 17.445)			
HDL-C %Change from Baseline at Month 12	6.35 (± 16.725)			
HDL-C %Change from Baseline at Month 24	11.73 (± 19.996)			
TC %Change from Baseline at Month 3	-29.6 (± 11.433)			
TC %Change from Baseline at Month 12	-33.91 (± 12.05)			
TC %Change from Baseline at Month 24	-32.03 (± 14.53)			
Triglycerides %Change from Baseline at Month 3	-7.95 (± 34.482)			
Triglycerides %Change from Baseline at Month 12	-7.85 (± 37.53)			
Triglycerides %Change from Baseline at Month 24	-0.12 (± 37.682)			
non-HDL C %Change from Baseline at Month 3	-36.35 (± 13.368)			
non-HDL C %Change from Baseline at Month 12	-41.66 (± 14.235)			
non-HDL C %Change from Baseline at Month 24	-40.4 (± 17.555)			
LDL-C/HDL-C %Change from Baseline at Month 3	-39.66 (± 17.381)			
LDL-C/HDL-C %Change from Baseline at Month 12	-45.63 (± 17.082)			
LDL-C/HDL-C %Change from Baseline at Month 24	-46.95 (± 20.126)			
TC/HDL-C %Change from Baseline at Month 3	-31.77 (± 14.874)			
TC/HDL-C %Change from Baseline at Month 12	-36.54 (± 14.474)			
TC/HDL-C %Change from Baseline at Month 24	-37.39 (± 17.079)			
Trig/HDL-C %Change from Baseline at Month 3	-9.05 (± 41.765)			
Trig/HDL-C %Change from Baseline at Month 12	-10.5 (± 40.633)			
Trig/HDL-C %Change from Baseline at Month 24	-7.12 (± 40.585)			
non-HDL-C/HDL-C %Change from Baseline at Month 3	-37.98 (± 17.369)			
non-HDL-C/HDL-C %Change from Baseline at Month 12	-43.71 (± 16.731)			
non-HDL-C/HDL-C %Change from Baseline at Month 24	-44.74 (± 19.896)			

ApoA-I %Change from Baseline at Month 3	4.77 (± 14.68)			
ApoA-I %Change from Baseline at Month 12	1.41 (± 13.747)			
ApoA-I %Change from Baseline at Month 24	2.34 (± 15.027)			
ApoB %Change from Baseline at Month 3	-29.29 (± 12.456)			
ApoB %Change from Baseline at Month 12	-35.65 (± 12.424)			
ApoB %Change from Baseline at Month 24	-35.72 (± 15.71)			
ApoB/ApoA-I %Change from Baseline at Month 3	-31.3 (± 15.524)			
ApoB/ApoA-I %Change from Baseline at Month 12	-35.66 (± 13.92)			
ApoB/ApoA-I %Change from Baseline at Month 24	-35.94 (± 18.743)			
hsCRP %Change from Baseline at Month 3	512.57 (± 4724.249)			
hsCRP %Change from Baseline at Month 12	42.96 (± 226.954)			
hsCRP %Change from Baseline at Month 24	98.36 (± 565.444)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Max and Mean carotid intima and media wall thickness (cIMT)

End point title	Change from Baseline in Max and Mean carotid intima and media wall thickness (cIMT)

End point description:

One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.

End point type	Secondary

End point timeframe:

At Month 12 and Month 24

End point values	Rosuvastatin	Healthy Siblings		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	64		
Units: mm				
arithmetic mean (standard deviation)				
Max cIMT Change from Baseline at Month 12	0.00626 (± 0.073446)	0.01707 (± 0.056223)		
Max cIMT Change from Baseline at Month 24	0.00189 (± 0.060864)	0.01202 (± 0.049102)		
Mean cIMT Change from Baseline at Month 12	0.00282 (± 0.041186)	0.01564 (± 0.032052)		

Mean cIMT Change from Baseline at Month 24	0.01056 (± 0.040762)	0.02779 (± 0.031004)		

Statistical analyses

No statistical analyses for this end point

Secondary: Adverse Events

End point title	Adverse Events

End point description:

Number of participants with Various Categories of AE's. One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.

End point type	Secondary

End point timeframe:

2-year study period

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Participant				
Any AE	172			
AE Leading to Death	0			
AE Leading to Discontinuation	3			
Serious AE	9			
Treatment Related AE	29			
Treatment Related AE Leading to Death	0			
Treatment Related AE Leading to Discontinuation	3			
Treatment Related Serious AE	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Total duration of exposure

End point title	Total duration of exposure

End point description:

Total duration of exposure was calculated as [last dose date of rosuva - first dose date of rosuva + 1 day]. One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.

End point type	Secondary

End point timeframe:

2-year study period

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Days				
arithmetic mean (standard deviation)	703.5 (± 97.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Height

End point title	Percent Change from Baseline in Height

End point description:

One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.

End point type	Secondary

End point timeframe:

At Month 12 and Month 24

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Percent change				
arithmetic mean (standard deviation)				
%Change from Baseline at Month 12	3.2 (± 2.023)			
%Change from Baseline at Month 24	5.91 (± 3.968)			

Statistical analyses

No statistical analyses for this end point

Secondary: Sexual Maturation by Tanner Staging at month 12

End point title	Sexual Maturation by Tanner Staging at month 12

End point description:

Tanner stages (I-V) was used to characterize physical development in children and adolescent. The stages was based on external primary and secondary sex characteristics, such as the size of the breasts, genitalia, and development of pubic hair. Tanner stage is considered going up when the organs grow bigger.

End point type	Secondary

End point timeframe:

At Baseline

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Participants				
Tanner Stage I at Month 12	61			
Tanner Stage II at Month 12	31			
Tanner Stage III at Month 12	21			
Tanner Stage IV at Month 12	32			
Tanner Stage V at Month 12	42			
Not Recorded at Month 12	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Sexual Maturation by Tanner Staging at month 24

End point title	Sexual Maturation by Tanner Staging at month 24

End point description:

Tanner stages (I-V) was used to characterize physical development in children and adolescent. The stages was based on external primary and secondary sex characteristics, such as the size of the breasts, genitalia, and development of pubic hair. Tanner stage is considered going up when the organs grow bigger.

End point type	Secondary

End point timeframe:

At Baseline

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Participants				
Tanner Stage I at Month 24	43			
Tanner Stage II at Month 24	33			
Tanner Stage III at Month 24	23			
Tanner Stage IV at Month 24	32			
Tanner Stage V at Month 24	64			
Not Recorded at Month 24	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Single Dose PK - Tmax

End point title	Single Dose PK - Tmax

End point description:

Serial plasma samples were taken at baseline (Week 0) at: 0.5 hours pre-dose and at 0.5, 1, 2, 3, 4, 5, 6, 9, 12 hours and on Day 1 at 24 hours after the single 10 mg dosing

End point type	Secondary

End point timeframe:

Serial blood samples over 24 hours

End point values	Single dose PK			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: hr				
arithmetic mean (standard deviation)	2.664 (± 1.8851)			

Statistical analyses

No statistical analyses for this end point

Secondary: Single Dose PK - AUC(0-24)

End point title	Single Dose PK - AUC(0-24)

End point description:

Serial plasma samples were taken at baseline (Week 0) at: 0.5 hours pre-dose and at 0.5, 1, 2, 3, 4, 5, 6, 9, 12 hours and on Day 1 at 24 hours after the single 10 mg dosing

End point type	Secondary

End point timeframe:

Serial blood samples over 24 hours

End point values	Single dose PK			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: ng*hr/mL				
arithmetic mean (standard deviation)	27.675 (± 26.6417)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overal treatment adherence

End point title	Overal treatment adherence

End point description:

Overall adherence rate was calculated as the weighted mean of adherence rates of all consecutive visits after baseline, in which the adherence rate between 2 consecutive visits was a percentage of the number of rosuvastatin taken divided by duration of exposure. One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.

End point type	Secondary

End point timeframe:

2-year study period

End point values	Rosuvastatin			
Subject group type	Reporting group			
Number of subjects analysed	197			
Units: Percent of doses				
arithmetic mean (standard deviation)	89.6 (± 12.25)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment Phase	
Adverse event reporting additional description:	
One patient received 1 dose of study drug but was not included in the efficacy and safety analyses due to a lack of follow-up data.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Rosuvastatin
Reporting group description:	
Rosuvastatin 5 mg, 10 mg or 20 mg	

Serious adverse events	Rosuvastatin		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 197 (4.57%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Urinary retention postoperative			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple fractures			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leg fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Pectus carinatum				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Epilepsy				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Streptococcal toxic shock syndrome				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral pericarditis				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 197 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	Rosuvastatin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	172 / 197 (87.31%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Vascular disorders			
Haematoma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 197 (3.55%)		
occurrences (all)	8		
Influenza like illness			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 197 (8.12%)		
occurrences (all)	19		
Malaise			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 197 (5.08%)		
occurrences (all)	10		
Immune system disorders			
Allergy to animal			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 197 (2.03%)		
occurrences (all)	4		
Seasonal allergy			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 197 (2.03%)		
occurrences (all)	4		
Reproductive system and breast disorders			
Amenorrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Dysmenorrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Menstrual disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Menstruation irregular			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Polycystic ovaries			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Scrotal pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	11		
Epistaxis			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 197 (3.05%)		
occurrences (all)	9		
Nasal congestion			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	3		
Nasal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Oropharyngeal pain			
alternative assessment type: Systematic			

subjects affected / exposed	13 / 197 (6.60%)		
occurrences (all)	13		
Rhinorrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 197 (2.54%)		
occurrences (all)	5		
Sinus disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Sinus congestion			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	4		
Psychiatric disorders			
Attention deficit/hyperactivity disorder			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Depressed mood			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Autism spectrum disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Depression			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Insomnia			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Intentional self-injury			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Sleep disorder			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Investigations			
Blood bilirubin increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 197 (2.03%)		
occurrences (all)	5		
Cardiac murmur			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	3		
Haemoglobin decreased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Hepatic enzyme increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	2		
Lymphocyte count abnormal			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Renal bruit			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Weight decreased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Serum ferritin decreased			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Arthropod bite			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Concussion			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	3		
Contusion			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Excoriation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	2		
Face injury			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Fall				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	4			
Femur fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Foot fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Forearm fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Hand fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Joint injury				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Laceration				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	2			
Ligament rupture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			

Ligament sprain				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 197 (2.54%)			
occurrences (all)	5			
Limb injury				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Lower limb fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Multiple fractures				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	2			
Muscle strain				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Periorbital haematoma				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Post procedural complication				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Post procedural swelling				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Post-traumatic pain				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Procedural pain				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	3			
Road traffic accident				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Scratch				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Tendon rupture				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	2			
Tendon injury				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	2			
Traumatic haematoma				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Urinary retention postoperative				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Wrist fracture				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	3			

Congenital, familial and genetic disorders			
Pectus carinatum			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 197 (3.05%)		
occurrences (all)	8		
Epilepsy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	4		
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	46 / 197 (23.35%)		
occurrences (all)	76		
Migraine			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	11		
Paraesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Post-traumatic headache			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Presyncope			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Psychomotor hyperactivity			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Syncope			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 197 (3.05%)		
occurrences (all)	11		
Blood and lymphatic system disorders			
Lymphadenopathy			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Auricular swelling			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Deafness unilateral			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Ear discomfort			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Ear pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Middle ear effusion			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Motion sickness			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Eye disorders			
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Myopia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Optic nerve disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	3		
Abdominal distension			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 197 (6.60%)		
occurrences (all)	18		
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 197 (7.61%)		
occurrences (all)	21		
Constipation			
alternative assessment type: Systematic			

subjects affected / exposed	4 / 197 (2.03%)			
occurrences (all)	4			
Dental discomfort				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Diarrhoea				
alternative assessment type: Systematic				
subjects affected / exposed	6 / 197 (3.05%)			
occurrences (all)	9			
Dyspepsia				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	4			
Flatulence				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	2			
Gastritis				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences (all)	6			
Intestinal obstruction				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Mouth ulceration				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Irritable bowel syndrome				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			

Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 197 (9.14%)		
occurrences (all)	24		
Toothache			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 197 (2.03%)		
occurrences (all)	4		
Rectal spasm			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 197 (9.64%)		
occurrences (all)	24		
Hepatobiliary disorders			
Hepatic pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 197 (3.05%)		
occurrences (all)	8		
Eczema			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 197 (2.03%)		
occurrences (all)	4		
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Pruritus			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Nail disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	3		
Rash vesicular			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Skin lesion			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Xanthoma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Pollakiuria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Polyuria			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	2		
Pyuria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Endocrine disorders			
Early menarche			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 197 (6.09%)		
occurrences (all)	15		
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 197 (3.05%)		
occurrences (all)	6		
Bone disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Exostosis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Flank pain			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Growing pains				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	4			
Joint stiffness				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Joint swelling				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Muscular weakness				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Muscle spasms				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	3			
Musculoskeletal pain				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences (all)	4			
Musculoskeletal stiffness				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences (all)	5			
Neck pain				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	2			

Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	12		
Osteochondrosis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Pain in extremity			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 197 (3.55%)		
occurrences (all)	7		
Pain in jaw			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Scoliosis			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 197 (1.52%)		
occurrences (all)	3		
Tendon disorder			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Tendon pain			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 197 (2.03%)		
occurrences (all)	4		
Tendonitis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Infections and infestations			

Amoebic dysentery				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Appendicitis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Bronchitis				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	3			
Conjunctivitis infective				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Cystitis				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	5			
Ear infection				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences (all)	5			
Furuncle				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Eye infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Gastritis viral				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Gastroenteritis				
alternative assessment type: Systematic				
subjects affected / exposed	12 / 197 (6.09%)			
occurrences (all)	15			
Gastroenteritis viral				
alternative assessment type: Systematic				
subjects affected / exposed	18 / 197 (9.14%)			
occurrences (all)	24			
Gingival infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Groin infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Herpes zoster				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Impetigo				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	3			
Infectious mononucleosis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Influenza				
alternative assessment type: Systematic				
subjects affected / exposed	20 / 197 (10.15%)			
occurrences (all)	28			

Laryngitis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Lower respiratory tract infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Mononucleosis syndrome				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Nail infection				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Nasopharyngitis				
alternative assessment type: Systematic				
subjects affected / exposed	88 / 197 (44.67%)			
occurrences (all)	150			
Otitis externa				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	2			
Otitis media				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	3			
Pertussis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Pharyngitis				
alternative assessment type: Systematic				

subjects affected / exposed	8 / 197 (4.06%)			
occurrences (all)	10			
Pharyngitis streptococcal				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Pilonidal cyst				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Pneumonia				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	2			
Pyelonephritis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Respiratory tract infection				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 197 (1.52%)			
occurrences (all)	3			
Rhinitis				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 197 (0.51%)			
occurrences (all)	1			
Sinusitis				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 197 (1.02%)			
occurrences (all)	4			
Tonsillitis				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 197 (2.03%)			
occurrences (all)	6			

Tooth infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Toxic shock syndrome streptococcal			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 197 (5.58%)		
occurrences (all)	12		
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 197 (3.55%)		
occurrences (all)	7		
Viral infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Viral pericarditis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 197 (1.02%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hypoglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 197 (0.51%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2010	Administrative changes/ updates
21 May 2010	Administrative changes/ updates
08 December 2010	Administrative changes/ updates
06 April 2011	Additional safety assessment required by US IRB

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported