Clinical trial results:
A Multi-Centre, Randomised, Double Blind, Placebo Controlled, Parallel Group Study of TA 8995 in Patients with Mild Dyslipidaemia, Alone and In Combination with Statin Therapy

Summary

EudraCT number	2012-005643-24
Trial protocol	NL DK
Global end of trial date	14 July 2014

Results information

Result version number	v1 (current)
This version publication date	21 March 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	TA-8995-03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01970215
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Xention Ltd
Sponsor organisation address	Iconix Park, London Road, Pampisford, Cambridge, United Kingdom, CB22 3EG
Public contact	Development, Xention Ltd, +44 1223 493900, info@xention.com
Scientific contact	Development, Xention Ltd, +44 1223 493900, info@xention.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 July 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 July 2014
Global end of trial reached?	Yes
Global end of trial date	14 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to evaluate the efficacy of TA 8995, alone and in combination with statin therapy, on the elevation of HDL C and reduction of LDL C following 12 weeks of treatment.

Protection of trial subjects:

No specific measures other than DSMB

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 August 2013
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	Netherlands: 331
Country: Number of subjects enrolled	Denmark: 33
Worldwide total number of subjects	364
EEA total number of subjects	364

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)	158
From 65 to 84 years	206
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening Period - Day -56 or -48 (depending on washout period required)
Run-in/Washout Period - Days -49 to -45

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

0mg TA-8995 & Placebo Statin

Arm type	Placebo
Investigational medicinal product name	TA-8995 0mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg TA-8995 (placebo)
1 capsule daily with food

Investigational medicinal product name	Placebo Statin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg Statin Placebo
1 capsule daily with food

Arm title	Group 2

Arm description:

1mg TA-8995 & Placebo Statin

Arm type	Experimental
Investigational medicinal product name	TA-8995 1mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1mg TA-8995
1 capsule daily with food

Investigational medicinal product name	Placebo Statin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg Statin Placebo
1 capsule daily with food

Arm title	Group 3

Arm description:

2.5mg TA-8995 & Placebo Statin

Arm type	Experimental
Investigational medicinal product name	TA-8995 2.5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

2.5mg TA-8995
1 capsule daily with food

Investigational medicinal product name	Placebo Statin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg Statin Placebo
1 capsule daily with food

Arm title	Group 4

Arm description:

5mg TA-8995 & Placebo Statin

Arm type	Experimental
Investigational medicinal product name	Placebo Statin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg Statin Placebo
1 capsule daily with food

Investigational medicinal product name	TA-8995 5mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5mg TA-8995
1 capsule daily with food

Arm title	Group 5

Arm description:

10mg TA-8995 & Placebo Statin

Arm type	Experimental

Investigational medicinal product name	Placebo Statin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg Statin Placebo
1 capsule daily with food

Investigational medicinal product name	TA-8995 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10mg TA-8995
1 capsule daily with food

Arm title	Group 6

Arm description:

0mg TA-8995 & 20mg Atorvastatin

Arm type	Active comparator
Investigational medicinal product name	TA-8995 0mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg TA-8995 (placebo)
1 capsule daily with food

Investigational medicinal product name	Atorvastatin 20mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20mg Atorvastatin
1 capsule daily with food

Arm title	Group 7

Arm description:

10mg TA-8995 & 20mg Atorvastatin

Arm type	Experimental
Investigational medicinal product name	TA-8995 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10mg TA-8995
1 capsule daily with food

Investigational medicinal product name	Atorvastatin 20mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20mg Atorvastatin
1 capsule daily with food

Arm title	Group 8
Arm description:	
0mg TA-8995 & 10mg Rosuvastatin	
Arm type	Active comparator
Investigational medicinal product name	TA-8995 0mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0mg TA-8995 (placebo)
1 capsule daily with food

Investigational medicinal product name	Rosuvastatin 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10mg Rosuvastatin
1 capsule daily with food

Arm title	Group 9
Arm description:	
10mg TA-8995 & 10mg Rosuvastatin	
Arm type	Experimental
Investigational medicinal product name	TA-8995 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10mg TA-8995
1 capsule daily with food

Investigational medicinal product name	Rosuvastatin 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10mg Rosuvastatin
1 capsule daily with food

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	40	41	41
Completed	37	37	38
Not completed	3	4	3
Consent withdrawn by subject	-	-	1
Physician decision	-	-	-
Adverse event, non-fatal	3	3	2
Not known	-	1	-
Protocol deviation	-	-	-

Number of subjects in period 1	Group 4	Group 5	Group 6
Started	40	40	40
Completed	39	35	36
Not completed	1	5	4
Consent withdrawn by subject	-	-	-
Physician decision	-	-	1
Adverse event, non-fatal	1	4	3
Not known	-	1	-
Protocol deviation	-	-	-

Number of subjects in period 1	Group 7	Group 8	Group 9
Started	40	41	41
Completed	38	38	39
Not completed	2	3	2
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	1	2	-
Not known	-	1	2
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	364	364	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	158	158	
From 65-84 years	206	206	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	67	67	
Male	297	297	

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description: 0mg TA-8995 & Placebo Statin	
Reporting group title	Group 2
Reporting group description: 1mg TA-8995 & Placebo Statin	
Reporting group title	Group 3
Reporting group description: 2.5mg TA-8995 & Placebo Statin	
Reporting group title	Group 4
Reporting group description: 5mg TA-8995 & Placebo Statin	
Reporting group title	Group 5
Reporting group description: 10mg TA-8995 & Placebo Statin	
Reporting group title	Group 6
Reporting group description: 0mg TA-8995 & 20mg Atorvastatin	
Reporting group title	Group 7
Reporting group description: 10mg TA-8995 & 20mg Atorvastatin	
Reporting group title	Group 8
Reporting group description: 0mg TA-8995 & 10mg Rosuvastatin	
Reporting group title	Group 9
Reporting group description: 10mg TA-8995 & 10mg Rosuvastatin	

Primary: % change in HDL-C levels from baseline to week 12

End point title	% change in HDL-C levels from baseline to week 12
End point description:	
End point type	Primary
End point timeframe: Baseline to week 12	

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	37	38	39
Units: Percentage				
arithmetic mean (standard deviation)	1.8 (± 10.974)	76.04 (± 26.35)	122.28 (± 41.391)	160.9 (± 42.269)

End point values	Group 5	Group 6	Group 7	Group 8
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	37	38	38
Units: Percentage				
arithmetic mean (standard deviation)	180.64 (± 42.111)	1.27 (± 10.941)	154.19 (± 48.988)	6.16 (± 12.87)

End point values	Group 9			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Percentage				
arithmetic mean (standard deviation)	159.86 (± 48.097)			

Statistical analyses

Statistical analysis title	Mixed Model for Repeated Measures (MMRM)

Statistical analysis description:

A restricted maximum likelihood mixed model for repeated measures (MMRM) approach was used. Analysis included fixed categorical effects of treatment, visit, and treatment-by-visit interaction, as well as a continuous fixed covariate for baseline HDL-C or LDL-C score.

Comparison groups	Group 1 v Group 2 v Group 3 v Group 4 v Group 5 v Group 6 v Group 7 v Group 8 v Group 9
Number of subjects included in analysis	337
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis

Primary: % change in LDL-C levels from baseline to week 12

End point title	% change in LDL-C levels from baseline to week 12

End point description:

End point type	Primary

End point timeframe:

Baseline to week 12

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	36	38	39
Units: percentage				
arithmetic mean (standard deviation)	-0.76 (± 11.858)	-26.96 (± 13.542)	-32.35 (± 16.259)	-45.08 (± 14.779)

End point values	Group 5	Group 6	Group 7	Group 8
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	37	38	38
Units: percentage				
arithmetic mean (standard deviation)	-45.01 (± 15.602)	-46.36 (± 12.068)	-67.8 (± 11.505)	-45.86 (± 10.202)

End point values	Group 9			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: percentage				
arithmetic mean (standard deviation)	-63.68 (± 9.901)			

Statistical analyses

Statistical analysis title	Mixed Model for Repeated Measures (MMRM)

Statistical analysis description:

A restricted maximum likelihood mixed model for repeated measures (MMRM) approach was used. Analysis included fixed categorical effects of treatment, visit, and treatment-by-visit interaction, as well as a continuous fixed covariate for baseline HDL-C or LDL-C score.

Comparison groups	Group 1 v Group 2 v Group 3 v Group 4 v Group 5 v Group 6 v Group 7 v Group 8 v Group 9
Number of subjects included in analysis	334
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Mixed models analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From informed consent to patients last visit.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	Group 1
Reporting group description: 0mg TA-8995 & Placebo Statin	
Reporting group title	Group 2
Reporting group description: 1mg TA-8995 & Placebo Statin	
Reporting group title	Group 3
Reporting group description: 2.5mg TA-8995 & Placebo Statin	
Reporting group title	Group 4
Reporting group description: 5mg TA-8995 & Placebo Statin	
Reporting group title	Group 5
Reporting group description: 10mg TA-8995 & Placebo Statin	
Reporting group title	Group 6
Reporting group description: 0mg TA-8995 & 20mg Atorvastatin	
Reporting group title	Group 7
Reporting group description: 10mg TA-8995 & 20mg Atorvastatin	
Reporting group title	Group 8
Reporting group description: 0mg TA-8995 & 10mg Rosuvastatin	
Reporting group title	Group 9
Reporting group description: 10mg TA-8995 & 10mg Rosuvastatin	

Serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	2 / 41 (4.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Renal neoplasm			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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
Cholangiocarcinoma			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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
Ovarian cyst			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Femoral hernia			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4	Group 5	Group 6
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	2 / 40 (5.00%)	1 / 40 (2.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal neoplasm			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 40 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	0 / 40 (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
Cholangiocarcinoma			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	0 / 40 (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
Ovarian cyst			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Femoral hernia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	0 / 40 (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	Group 7	Group 8	Group 9
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	1 / 41 (2.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal neoplasm			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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
Cholangiocarcinoma			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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
Ovarian cyst			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 41 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 41 (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
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
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			
Femoral hernia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (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

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 40 (80.00%)	32 / 41 (78.05%)	30 / 41 (73.17%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 40 (5.00%)	3 / 41 (7.32%)	2 / 41 (4.88%)
occurrences (all)	2	3	2
Headache			
subjects affected / exposed	7 / 40 (17.50%)	3 / 41 (7.32%)	8 / 41 (19.51%)
occurrences (all)	7	3	8

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 40 (7.50%)	0 / 41 (0.00%)	2 / 41 (4.88%)
occurrences (all)	3	0	2
Influenza like illness			
subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	3 / 41 (7.32%)
occurrences (all)	1	2	3
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 40 (0.00%)	3 / 41 (7.32%)	0 / 41 (0.00%)
occurrences (all)	0	3	0
Diarrhoea			
subjects affected / exposed	1 / 40 (2.50%)	3 / 41 (7.32%)	1 / 41 (2.44%)
occurrences (all)	1	3	1
Toothache			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	3 / 41 (7.32%)
occurrences (all)	1	1	3
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	3 / 41 (7.32%)
occurrences (all)	0	1	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences (all)	1	0	1
Back pain			
subjects affected / exposed	3 / 40 (7.50%)	1 / 41 (2.44%)	2 / 41 (4.88%)
occurrences (all)	3	1	2
Myalgia			
subjects affected / exposed	2 / 40 (5.00%)	2 / 41 (4.88%)	2 / 41 (4.88%)
occurrences (all)	2	2	2
Osteoarthritis			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	2 / 41 (4.88%)
occurrences (all)	1	2	2
Nasopharyngitis			
subjects affected / exposed	7 / 40 (17.50%)	9 / 41 (21.95%)	9 / 41 (21.95%)
occurrences (all)	7	9	9
Urinary tract infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	1 / 41 (2.44%)
occurrences (all)	0	1	1

Non-serious adverse events	Group 4	Group 5	Group 6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 40 (80.00%)	33 / 40 (82.50%)	30 / 40 (75.00%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 40 (2.50%)	1 / 40 (2.50%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Headache			
subjects affected / exposed	2 / 40 (5.00%)	8 / 40 (20.00%)	5 / 40 (12.50%)
occurrences (all)	2	8	5
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 40 (2.50%)	2 / 40 (5.00%)	1 / 40 (2.50%)
occurrences (all)	1	2	1
Influenza like illness			
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	2 / 40 (5.00%)
occurrences (all)	2	0	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	4 / 40 (10.00%)	2 / 40 (5.00%)	0 / 40 (0.00%)
occurrences (all)	4	2	0
Diarrhoea			
subjects affected / exposed	1 / 40 (2.50%)	2 / 40 (5.00%)	1 / 40 (2.50%)
occurrences (all)	1	2	1

Toothache			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 40 (5.00%)	0 / 40 (0.00%)	1 / 40 (2.50%)
occurrences (all)	2	0	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 40 (2.50%)	3 / 40 (7.50%)	2 / 40 (5.00%)
occurrences (all)	1	3	2
Back pain			
subjects affected / exposed	2 / 40 (5.00%)	2 / 40 (5.00%)	2 / 40 (5.00%)
occurrences (all)	2	2	2
Myalgia			
subjects affected / exposed	4 / 40 (10.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
occurrences (all)	4	1	0
Osteoarthritis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 40 (0.00%)	4 / 40 (10.00%)	1 / 40 (2.50%)
occurrences (all)	0	4	1
Nasopharyngitis			
subjects affected / exposed	13 / 40 (32.50%)	8 / 40 (20.00%)	10 / 40 (25.00%)
occurrences (all)	13	8	10
Urinary tract infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 40 (2.50%)	0 / 40 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Group 7	Group 8	Group 9
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	28 / 40 (70.00%)	33 / 41 (80.49%)	34 / 41 (82.93%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 41 (2.44%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	4 / 40 (10.00%)	5 / 41 (12.20%)	6 / 41 (14.63%)
occurrences (all)	4	5	6
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 40 (5.00%)	1 / 41 (2.44%)	1 / 41 (2.44%)
occurrences (all)	2	1	1
Influenza like illness			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	1 / 41 (2.44%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	4 / 40 (10.00%)	1 / 41 (2.44%)	2 / 41 (4.88%)
occurrences (all)	4	1	2
Toothache			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	0 / 41 (0.00%)
occurrences (all)	1	2	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	3 / 41 (7.32%)
occurrences (all)	1	1	3
Back pain			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	5 / 41 (12.20%)
occurrences (all)	1	1	5
Myalgia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	2 / 41 (4.88%)
occurrences (all)	0	1	2
Osteoarthritis			
subjects affected / exposed	0 / 40 (0.00%)	3 / 41 (7.32%)	0 / 41 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Influenza			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	3 / 41 (7.32%)
occurrences (all)	0	2	3
Nasopharyngitis			
subjects affected / exposed	14 / 40 (35.00%)	7 / 41 (17.07%)	3 / 41 (7.32%)
occurrences (all)	14	7	3
Urinary tract infection			
subjects affected / exposed	1 / 40 (2.50%)	4 / 41 (9.76%)	0 / 41 (0.00%)
occurrences (all)	1	4	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2013	Changes clarified the screening criteria, improved efficiency of the run-in/washout period, and made the safety procedures more robust
17 September 2013	Changes were made to improve the screening criteria and add the PCSK9 assay as an exploratory efficacy assessment. Changes were made to allow enrollment of women of childbearing potential, including a urine pregnancy test at screening.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26047975