Clinical trial results:
Exploratory study to assess the efficacy and safety of calcium pangamate in patients with type 2 diabetes mellitus and dyslipidemia treated with statins.

Summary

EudraCT number	2007-002568-89
Trial protocol	PT
Global end of trial date	07 January 2013

Results information

Result version number	v1 (current)
This version publication date	23 July 2020
First version publication date	23 July 2020

Trial information

Trial identification

Sponsor protocol code	NAS SIM-PAN II/2006/001/PT

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Tecnimede, Sociedade Técnico-Medicinal, S.A.
Sponsor organisation address	Zona Industrial da Abrunheira, R. da Tapada Grande, nº 2, Sintra, Portugal, 2710-089
Public contact	Head of Medical Department, Tecnimede - Sociedade Técnico-Medicinal, S.A., 00351 210 414 100, dmed.ct@tecnimede.pt
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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	07 January 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 January 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of Ca PGM 400 mg o.d. for 8 weeks as add-on treatment of statins (lovastatin, simvastatin, pravastatin, atorvastatin, fluvastatin or rosuvastatin) on HDL-C of patients with type 2 diabetes mellitus (DM) and dyslipidemia.

Protection of trial subjects:

This study was conducted in compliance with the Good Clinical Practice (GCP) of the International Council for Harmonisation (ICH), the World Medical Association's (WMA) principles of the Declaration of Helsinki, Directive 2001/20/EC of the European Parliament and the Council of 4 April 2001, Directive 2005/28/EC of the European Parliament and the Council of 8 April 2005 and the legislation to clinical trials on medicinal products for human use for Portugal at the time the study was conducted (Law 46/2004 of 19 August 2004).

Background therapy:

The trial design has been selected to allow comparison of the effects on HDL-C of a concomitant administration of a statin with Ca PGM versus a statin alone (combination with placebo of Ca PGM) in patients with type 2 diabetes mellitus and dyslipidemia. Therefore and in order to evaluate this effect, all the patients were being treated with statins (lovastatin, simvastatin, pravastatin, atorvastatin, fluvastatin or rosuvastatin) with no changes in treatment regimen in the 8 weeks prior to Visit 1.

Evidence for comparator: -

Actual start date of recruitment	18 February 2011
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	Portugal: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	35
From 65 to 84 years	25
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The start date of recruitment was on 18 February 2011 (1st screening failure) and the date of the last patient recruited was on 06-Nov-2012 (LPFV). Of the 94 patients selected in the screening phase, 60 were randomized into the study, but one patient did not initiate the IMP thus no information about the patient's condition was evaluated.

Pre-assignment

Screening details:

Period corresponding to approximately 14 days where the study patients kept the recommended diet and followed the prescribed hypoglycaemic and statin medication, comprised by 2 visits: V1 (week -2) and V2 (week -1; 1 week ± 2 days after V1). This period ended after the performance of all the required procedures to confirm patient's eligibility.

Period 1

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

Blinding implementation details:

Neither the patient nor the principal investigator, pharmaceutical services and staff involved in the clinical operations (sponsor and CRO) had access to the treatment being administered to each patient. The double blind was achieved through IMP coding, and not identifying, in the medication labels, the active substance of the IMPs, as well as due to the appearance of both IMPs which was the same as described in the corresponding certificates of analysis.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

Ca PGM 400 mg

Arm type	Experimental
Investigational medicinal product name	Calcium pangamate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients who were randomized, took 2 tablets of Ca PGM 200 mg in the morning (between 6:30 AM and 11:00 AM), fasting and in a single dose (400mg o.d.).

Arm title	Group B

Arm description:

Ca PGM Placebo

Arm type	Placebo
Investigational medicinal product name	Calcium pangamate placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Patients who were randomized, took 2 tablets of Ca PGM placebo in the morning (between 6:30 AM and 11:00 AM), fasting and in a single dose.

Number of subjects in period 1[1]	Group A	Group B
Started	30	29
Completed	27	27
Not completed	3	2
Patient incorrectly included in the study	1	-
Consent withdrawn by subject	1	1
Changes in lipid lowering/hypoglycemic therapies	1	-
Lost to follow-up	-	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: For this study 60 patients were randomized (31 patients in Group A (Ca PGM) and 29 patients in Group B (placebo)). However, patient D1803 after performing the study procedures of Visit 3 he/she did not initiate the study medication thus no information about the patient's condition or study medication intake was evaluated.

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description: Ca PGM 400 mg	
Reporting group title	Group B
Reporting group description: Ca PGM Placebo	

Reporting group values	Group A	Group B	Total
Number of subjects	30	29	59
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	20	14	34
From 65-84 years	10	15	25
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	61.90	63.72	
standard deviation	± 7.41	± 7.64	-
Gender categorical Units: Subjects			
Female	9	9	18
Male	21	20	41
Smoking habits Units: Subjects			
Yes	4	0	4
No	13	18	31
Ex-smoker	13	11	24
Drinking habits Units: Subjects			
Yes	10	9	19
No	20	20	40
Post-menopausal (only females) Units: Subjects			
Yes	9	9	18
No	0	0	0
NA	21	20	41
Sexual active (only females) Units: Subjects			

Yes	6	6	12
No	2	3	5
Unknown	1	0	1
NA	21	20	41
Height			
Units: meter			
arithmetic mean	1.66	1.65	
standard deviation	± 0.09	± 0.07	-
Heart rate			
Units: bpm			
arithmetic mean	71.20	72.79	
standard deviation	± 11.81	± 9.48	-
Systolic blood pressure			
Units: mm Hg			
arithmetic mean	133.17	131.38	
standard deviation	± 15.57	± 14.03	-
Diastolic blood pressure			
Units: mm Hg			
arithmetic mean	75.03	77.69	
standard deviation	± 10.34	± 11.53	-
Weight			
Units: kilogram(s)			
arithmetic mean	85.18	86.02	
standard deviation	± 12.27	± 12.78	-
Body mass index			
Units: kilogram(s)/square meter			
arithmetic mean	30.96	31.53	
standard deviation	± 4.34	± 3.85	-
Framingham risk score			
Units: Points			
arithmetic mean	13.93	14.24	
standard deviation	± 3.26	± 3.17	-
Framingham risk score (%)			
Units: 10-year risk			
arithmetic mean	12.61	12.29	
standard deviation	± 7.84	± 8.00	-

End points

End points reporting groups

Reporting group title	Group A
Reporting group description: Ca PGM 400 mg	
Reporting group title	Group B
Reporting group description: Ca PGM Placebo	
Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All patients who gave their informed consent and who were randomized were included. Randomized patients were excluded from the ITT analysis in case they fulfil at least one of the following criteria: patients who did not perform the treatment for at least one day; patients for whom it was not possible to collect any data following randomization.	
Subject analysis set title	PP population
Subject analysis set type	Per protocol
Subject analysis set description: Only subjects who were compliant with the protocol and were characterized by criteria such as the following would be included: the completion of a certain pre-specified minimal exposure to the treatment regimen, i.e., subjects who completed the 8 weeks treatment period; the absence of any major protocol violations including the violation of entry criteria; the availability of measurements of the efficacy variable to be evaluated.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description: All randomized patients who have completed at least one day of treatment and for whom it was possible to collect any data following randomization were included in the analysis. This population was also used to characterize the study population.	

Primary: Relative mean increase (%) in HDL-C vs. baseline following 8 weeks of treatment (ITT population).

End point title	Relative mean increase (%) in HDL-C vs. baseline following 8 weeks of treatment (ITT population).
End point description: HDL-C: High density lipoprotein-cholesterol.	
End point type	Primary
End point timeframe: Relative mean increase (%) in HDL-C vs. baseline following 8 weeks of treatment (ITT population).	

End point values	Group A	Group B	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28	28	56	
Units: HDL-C variation (%)				
arithmetic mean (standard deviation)	4.31 (± 10.64)	2.79 (± 9.39)	3.55 (± 9.97)	

Statistical analyses

Statistical analysis title	Relative mean increase (%) in HDL-C
Comparison groups	Group A v Group B
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.574
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	3.86

Primary: Relative mean increase (%) in HDL-C vs. baseline following 8 weeks of treatment (PP population).

End point title	Relative mean increase (%) in HDL-C vs. baseline following 8 weeks of treatment (PP population).
End point description:	
HDL-C: High density lipoprotein-cholesterol.	
End point type	Primary
End point timeframe:	
Relative mean increase (%) in HDL-C vs. baseline following 8 weeks of treatment (PP population).	

End point values	Group A	Group B	PP population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	23	25	48	
Units: HDL-C variation (%)				
arithmetic mean (standard deviation)	4.01 (± 10.89)	3.53 (± 9.55)	3.76 (± 10.11)	

Statistical analyses

Statistical analysis title	Relative mean increase (%) in HDL-C
Comparison groups	Group A v Group B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.872
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.46
upper limit	5.5

Secondary: Relative mean decrease (%) in TG vs. baseline following 8 weeks of treatment (ITT population).

End point title	Relative mean decrease (%) in TG vs. baseline following 8 weeks of treatment (ITT population).
End point description:	
TG: Triglycerides.	
End point type	Secondary
End point timeframe:	
Relative mean decrease (%) in TG vs. baseline following 8 weeks of treatment (ITT population).	

End point values	Group A	Group B	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28	28	56	
Units: TG variation (%)				
arithmetic mean (standard deviation)	11.65 (± 33.17)	3.72 (± 26.68)	7.69 (± 30.09)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in TG
Comparison groups	Group B v Group A
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.329
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-7.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.08
upper limit	8.22

Secondary: Relative mean decrease (%) in TG vs. baseline following 8 weeks of treatment (PP population).

End point title	Relative mean decrease (%) in TG vs. baseline following 8 weeks of treatment (PP population).

End point description:

TG: Triglycerides.

End point type	Secondary

End point timeframe:

Relative mean decrease (%) in TG vs. baseline following 8 weeks of treatment (PP population).

End point values	Group A	Group B	PP population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	23	25	48	
Units: TG variation (%)				
arithmetic mean (standard deviation)	9.10 (± 27.91)	-1.22 (± 21.18)	3.72 (± 24.91)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in TG
Comparison groups	Group A v Group B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.16
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-10.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.85
upper limit	4.22

Secondary: Relative mean decrease (%) in LDL-C vs. baseline following 8 weeks of treatment (ITT population).

End point title	Relative mean decrease (%) in LDL-C vs. baseline following 8 weeks of treatment (ITT population).

End point description:

LDL-C: Low density lipoprotein-cholesterol.

End point type	Secondary

End point timeframe:

Relative mean decrease (%) in LDL-C vs. baseline following 8 weeks of treatment (ITT population).

End point values	Group A	Group B	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	27	27	54	
Units: LDL-C variation (%)				
arithmetic mean (standard deviation)	2.28 (± 28.28)	8.52 (± 19.51)	5.40 (± 24.27)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in LDL-C
Comparison groups	Group A v Group B
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.35
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	6.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.06
upper limit	19.55

Secondary: Relative mean decrease (%) in LDL-C vs. baseline following 8 weeks of treatment (PP population).

End point title	Relative mean decrease (%) in LDL-C vs. baseline following 8 weeks of treatment (PP population).
End point description:	
LDL-C: Low density lipoprotein-cholesterol.	
End point type	Secondary
End point timeframe:	
Relative mean decrease (%) in LDL-C vs. baseline following 8 weeks of treatment (PP population).	

End point values	Group A	Group B	PP population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	22	24	46	
Units: LDL-C variation (%)				
arithmetic mean (standard deviation)	3.78 (± 30.99)	8.89 (± 19.78)	6.45 (± 25.59)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in LDL-C
Comparison groups	Group A v Group B
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.513
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	5.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	20.83

Secondary: Relative mean decrease (%) in TC vs. baseline following 8 weeks of treatment (ITT population).

End point title	Relative mean decrease (%) in TC vs. baseline following 8 weeks of treatment (ITT population).
End point description: TC: Total cholesterol.	
End point type	Secondary
End point timeframe: Relative mean decrease (%) in TC vs. baseline following 8 weeks of treatment (ITT population).	

End point values	Group A	Group B	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28	28	56	
Units: TC variation (%)				
arithmetic mean (standard deviation)	2.21 (± 17.70)	4.92 (± 13.00)	3.56 (± 15.44)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in TC
Comparison groups	Group A v Group B
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.517
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.63
upper limit	11.04

Secondary: Relative mean decrease (%) in TC vs. baseline following 8 weeks of treatment (PP population).

End point title	Relative mean decrease (%) in TC vs. baseline following 8 weeks of treatment (PP population).
End point description:	
TC: Total cholesterol.	
End point type	Secondary
End point timeframe:	
Relative mean decrease (%) in TC vs. baseline following 8 weeks of treatment (PP population).	

End point values	Group A	Group B	PP population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	23	25	48	
Units: TC variation (%)				
arithmetic mean (standard deviation)	2.46 (± 18.81)	4.44 (± 13.23)	3.49 (± 16.00)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in TC
Comparison groups	Group A v Group B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.678
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.59
upper limit	11.55

Secondary: Relative mean decrease (%) in TC/HDL-C ratio vs. baseline following 8 weeks of treatment (ITT population).

End point title	Relative mean decrease (%) in TC/HDL-C ratio vs. baseline

	following 8 weeks of treatment (ITT population).

End point description:

TC: Total cholesterol; HDL-C: High density lipoprotein-cholesterol.

End point type	Secondary

End point timeframe:

Relative mean decrease (%) in TC/HDL-C ratio vs. baseline following 8 weeks of treatment (ITT population).

End point values	Group A	Group B	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28	28	56	
Units: TC/HDL-C variation (%)				
arithmetic mean (standard deviation)	-1.83 (± 15.09)	3.57 (± 14.10)	0.87 (± 14.73)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in TC/HDL-C ratio
Comparison groups	Group A v Group B
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.172
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.43
upper limit	13.23

Secondary: Relative mean decrease (%) in TC/HDL-C ratio vs. baseline following 8 weeks of treatment (PP population).

End point title	Relative mean decrease (%) in TC/HDL-C ratio vs. baseline following 8 weeks of treatment (PP population).

End point description:

TC: Total cholesterol; HDL-C: High density lipoprotein-cholesterol.

End point type	Secondary

End point timeframe:

Relative mean decrease (%) in TC/HDL-C ratio vs. baseline following 8 weeks of treatment (PP population).

End point values	Group A	Group B	PP population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	23	25	48	
Units: TC/HDL-C variation (%)				
arithmetic mean (standard deviation)	-1.33 (± 16.10)	2.48 (± 14.32)	0.65 (± 15.16)	

Statistical analyses

Statistical analysis title	Relative mean decrease (%) in the TC/HDL-C ratio
Comparison groups	Group A v Group B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.392
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	3.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.07
upper limit	12.71

Secondary: Relative mean decrease (%) in non-HDL-C/HDL-C ratio vs. baseline following 8 weeks of treatment (ITT population).

End point title	Relative mean decrease (%) in non-HDL-C/HDL-C ratio vs. baseline following 8 weeks of treatment (ITT population).

End point description:

HDL-C: High density lipoprotein-cholesterol.

End point type	Secondary

End point timeframe:

Relative mean decrease (%) in non-HDL-C/HDL-C ratio vs. baseline following 8 weeks of treatment (ITT population).

End point values	Group A	Group B	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28	28	56	
Units: non-HDL-C/HDL-C variation (%)				
arithmetic mean (standard deviation)	-1.46 (± 19.68)	3.10 (± 18.81)	0.82 (± 19.21)	

Statistical analyses

Statistical analysis title	Relative mean decrease(%) in non-HDL-C/HDL-C ratio
Comparison groups	Group A v Group B
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.379
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	4.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.75
upper limit	14.88

Secondary: Relative mean decrease (%) in non-HDL-C/HDL-C ratio vs. baseline following 8 weeks of treatment (PP population).

End point title	Relative mean decrease (%) in non-HDL-C/HDL-C ratio vs. baseline following 8 weeks of treatment (PP population).

End point description:

HDL-C: High density lipoprotein-cholesterol.

End point type	Secondary

End point timeframe:

Relative mean decrease (%) in non-HDL-C/HDL-C ratio vs. baseline following 8 weeks of treatment (PP population).

End point values	Group A	Group B	PP population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	23	25	48	
Units: non-HDL-C/HDL-C variation (%)				
arithmetic mean (standard deviation)	-0.73 (± 21.12)	1.49 (± 19.00)	0.43 (± 19.86)	

Statistical analyses

Statistical analysis title	Relative mean decrease(%) in non-HDL-C/HDL-C ratio
Comparison groups	Group A v Group B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.705
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.5
upper limit	13.94

Secondary: Proportion of patients who have achieved the HDL-C goal of HDL-C > 45.0 mg/dL for males and > 55.0 mg/dL for females (ITT population).

End point title	Proportion of patients who have achieved the HDL-C goal of HDL-C > 45.0 mg/dL for males and > 55.0 mg/dL for females (ITT population).

End point description:

HDL-C: High density lipoprotein-cholesterol.

End point type	Secondary

End point timeframe:

Proportion of patients who have achieved the HDL-C goal of HDL-C > 45.0 mg/dL for males and > 55.0 mg/dL for females after 8 weeks of treatment (ITT population).

End point values	Group A	Group B	ITT population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	28	28	56	
Units: Patients				
Yes	4	4	8	
No	24	24	48	

Statistical analyses

Statistical analysis title	Proportion of patients who achieved HDL-C goal
Comparison groups	Group A v Group B

Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Secondary: Proportion of patients who have achieved the HDL-C goal of HDL-C > 45.0 mg/dL for males and > 55.0 mg/dL for females (PP population).

End point title	Proportion of patients who have achieved the HDL-C goal of HDL-C > 45.0 mg/dL for males and > 55.0 mg/dL for females (PP population).

End point description:

HDL-C: High density lipoprotein-cholesterol.

End point type	Secondary

End point timeframe:

Proportion of patients who have achieved the HDL-C goal of HDL-C > 45.0 mg/dL for males and > 55.0 mg/dL for females after 8 weeks of treatment (PP population).

End point values	Group A	Group B	PP population	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	23	25	48	
Units: Patients				
Yes	3	4	7	
No	20	21	41	

Statistical analyses

Statistical analysis title	Proportion of patients who achieved the HDL-C goal
Comparison groups	Group A v Group B
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the study, it was the responsibility of the investigator to collect all AEs (both serious and non-serious) and to notify the sponsor of these events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Group A
Reporting group description: -	
Reporting group title	Group B

Reporting group description: -

Serious adverse events	Group A	Group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)	2 / 29 (6.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Group A	Group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 30 (26.67%)	10 / 29 (34.48%)	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Phlebitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Nervousness			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Anxiety			

subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Investigations			
Low density lipoprotein increased			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Red blood cell sedimentation rate increased			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 30 (3.33%)	1 / 29 (3.45%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Nervous system disorders			
Somnolence			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Eye disorders			

Visual impairment			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Gastrointestinal pain			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Leukocyturia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Eye infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Gout			

subjects affected / exposed	0 / 30 (0.00%)	1 / 29 (3.45%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 29 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2010	The study sample size has been updated; the randomization procedures have been updated to reflect the change on study sample size.
26 March 2010	Change from single blind study to double blind study; update of schedule of events by removing the AEs assessment during the screening period (V1 and V2) and replacing the assessment of cardiovascular disease risk factors by assessment of coronary heart disease risk factors; it has been added a reference indicating that patient's toxic habits would also be collected as demographic data; replacement of assessment of cardiovascular disease risk factors by assessment of coronary heart disease risk factors, performed using the Framingham score; total cholesterol has been added as a laboratory parameter for lipid profile; it has been added a reference regarding the possibility for unblinding in case of the occurrence of SAEs which could jeopardize patient's safety.
21 June 2010	Clarification of the withdrawal criterion nº 2 in order to specify which laboratory values changes are considered for study withdrawal; a new withdrawal criterion (13. Unknown) has been added to describe those situations where the contact with the patient is lost.
09 June 2011	Corrections performed in the concomitant medication section (allowed and prohibited) in order to be in accordance with the information mentioned in the inclusion/exclusion criteria and other sections of the protocol; it has been removed the mention to diet from sections of study design and schedule of events in order to be in accordance with the information mentioned in the inclusion criteria and other sections of the protocol.
09 September 2011	Removal of an inclusion criterion concerning the range of serum concentration of triglycerides (>150,0 and < 500,0 mg/dl).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported