



Clinical trial results:

A Phase 2b, Multi-center, Randomized, Placebo-controlled, Dose-ranging Study to Investigate the Safety and Tolerability of Multiple Dose Administration of CSL112 in Subjects with Acute Myocardial Infarction Summary

EudraCT number	2013-003458-26
Trial protocol	DE GB IT CZ AT DK HU NL ES FR
Global end of trial date	21 March 2016

Results information

Result version number	v1 (current)
This version publication date	22 March 2017
First version publication date	22 March 2017

Trial information

Trial identification

Sponsor protocol code	CSLCT-HDL-12-77
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02108262
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring LLC
Sponsor organisation address	1020 First Avenue, King of Prussia, United States, 19406
Public contact	Clin.Trial Registration Coordinator, CSL Behring, clinicaltrials@cslbehring.com
Scientific contact	Clin.Trial Registration Coordinator, CSL Behring, clinicaltrials@cslbehring.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	13 July 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the hepatic and renal safety of multiple dose administration of two dose levels of CSL112 (low dose [2 g] or high dose [6 g]) compared with placebo in subjects with acute myocardial infarction.

Protection of trial subjects:

Before undergoing screening procedures for possible enrollment into the study, subjects were informed, in an understandable form, about the nature, scope, and possible consequences of the study. The investigator was responsible for obtaining a subject's written informed consent to participate in the study. The investigator may cease study treatment and withdraw the subject, or the subject may withdraw himself from participation in the study at any time. In accordance with International Conference on Harmonisation principles of Good Clinical Practice, the Investigator always had the option to advise a subject to stop further administration of investigational product (IP) if the subject's safety or well-being was compromised by the continued administration of IP. Concern for the interests of the subject was always to prevail over the interests of the study. However, subjects were to continue to be followed for safety and the occurrence of Major Adverse Cardiovascular Events (MACE). At minimum, all efforts were to be made to confirm vital status if a subject was unwilling or unable to return for scheduled on-site visits or refused to be contacted by telephone for the MACE follow-up visits.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 August 2014
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: 145
Country: Number of subjects enrolled	Poland: 204
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Bulgaria: 140
Country: Number of subjects enrolled	Czech Republic: 104
Country: Number of subjects enrolled	Denmark: 28
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 86
Country: Number of subjects enrolled	Hungary: 202
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Canada: 25

Country: Number of subjects enrolled	Israel: 81
Country: Number of subjects enrolled	United States: 167
Worldwide total number of subjects	1258
EEA total number of subjects	967

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)	903
From 65 to 84 years	350
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

A safety lead-in was conducted before enrollment into the main study, and provided an early assessment of safety in subjects with acute myocardial infarction and mild renal impairment or normal renal function. Upon confirmation of safety in the lead-in, additional subjects were screened for enrollment in the main study.

Pre-assignment

Screening details:

A total of 11 subjects were screened for participation in the safety lead-in, and 9 subjects were enrolled. A total of 1401 subjects were screened for entry into the main study. Of these subjects, 143 subjects were screen failures, and the remaining 1258 eligible subjects were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	CSL112 (2 g)

Arm description:

CSL112 (low dose) is to be administered as an intravenous (IV) infusion once weekly for 4 consecutive weeks.

Arm type	Experimental
Investigational medicinal product name	CSL112
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CSL112 (low or high dose) is to be administered as an intravenous (IV) infusion once weekly for 4 consecutive weeks.

Arm title	CSL112 (6 g)
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Arm description:

CSL112 (high dose) is to be administered as an IV infusion once weekly for 4 consecutive weeks.

Arm type	Experimental
Investigational medicinal product name	CSL112
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

CSL112 (low or high dose) is to be administered as an intravenous (IV) infusion once weekly for 4 consecutive weeks.

Arm title	Placebo
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Arm description:

Placebo is to be administered as an IV infusion at the same frequency, volume and duration as either the low dose or high dose CSL112 infusion.

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo (0.9% weight/volume sodium chloride solution (ie, normal saline) is to be administered as an IV infusion at the same frequency, volume and duration as either the low dose or high dose CSL112 infusion.

Number of subjects in period 1	CSL112 (2 g)	CSL112 (6 g)	Placebo
Started	419	421	418
Completed	375	379	376
Not completed	44	42	42
Adverse event, serious fatal	2	2	1
Physician decision	-	2	-
Patient did not want another infusion	3	3	2
Randomized by error/screen failure	-	1	-
Consent withdrawn by subject	7	3	4
Patient decision	7	9	14
Adverse event, non-fatal	11	6	12
Due to key hepatic values	1	-	-
Missed IV due to pharmacy error	-	1	-
Non-compliance	2	1	1
Vacation	1	-	-
Unable to contact patient	3	1	2
Patient unable to come to site/attend visit	6	11	6
Lost to follow-up	-	1	-
Distance to center	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	CSL112 (2 g)
Reporting group description: CSL112 (low dose) is to be administered as an intravenous (IV) infusion once weekly for 4 consecutive weeks.	
Reporting group title	CSL112 (6 g)
Reporting group description: CSL112 (high dose) is to be administered as an IV infusion once weekly for 4 consecutive weeks.	
Reporting group title	Placebo
Reporting group description: Placebo is to be administered as an IV infusion at the same frequency, volume and duration as either the low dose or high dose CSL112 infusion.	

Reporting group values	CSL112 (2 g)	CSL112 (6 g)	Placebo
Number of subjects	419	421	418
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)	306	296	301
From 65-84 years	111	124	115
85 years and over	2	1	2
Age continuous Units: years			
arithmetic mean	57.7	59.2	58.1
standard deviation	± 10.15	± 9.87	± 10.57
Gender categorical Units: Subjects			
Female	82	98	77
Male	337	323	341
Renal function from Interactive Web Response System (IWRS) Units: Subjects			
Normal renal function	195	192	191
Mild renal impairment	224	229	227

Reporting group values	Total		
Number of subjects	1258		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	903		
From 65-84 years	350		
85 years and over	5		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	257		
Male	1001		
Renal function from Interactive Web Response System (IWRS)			
Units: Subjects			
Normal renal function	578		
Mild renal impairment	680		

End points

End points reporting groups

Reporting group title	CSL112 (2 g)
Reporting group description: CSL112 (low dose) is to be administered as an intravenous (IV) infusion once weekly for 4 consecutive weeks.	
Reporting group title	CSL112 (6 g)
Reporting group description: CSL112 (high dose) is to be administered as an IV infusion once weekly for 4 consecutive weeks.	
Reporting group title	Placebo
Reporting group description: Placebo is to be administered as an IV infusion at the same frequency, volume and duration as either the low dose or high dose CSL112 infusion.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety population comprised all subjects who were randomized into the main study or PK/PD substudy and received at least a partial infusion of the IP.	
Subject analysis set title	ITT population
Subject analysis set type	Intention-to-treat
Subject analysis set description: The Intent-to-Treat (ITT) population comprised all subjects who were randomized to one of the three treatment groups for the Main Study or PK/PD substudy.	
Subject analysis set title	Pharmacokinetic (PK) population
Subject analysis set type	Intention-to-treat
Subject analysis set description: The PK population comprised all subjects who received at least 1 infusion of IP and had at least 1 post baseline measurable plasma concentration of apoA-I or PC.	
Subject analysis set title	Pharmacokinetic/Pharmacodynamic (PK/PD) population
Subject analysis set type	Sub-group analysis
Subject analysis set description: The Pharmacokinetic/Pharmacodynamic (PK/PD) population was a subset of subjects from the main study who consented to participate in the PK/PD substudy.	
Subject analysis set title	Serology population
Subject analysis set type	Sub-group analysis
Subject analysis set description: A random subset of subjects was selected and had their samples tested for the presence of parvovirus B19.	

Primary: Percent of subjects with clinically important change in drug-induced liver injury (Safety population)

End point title	Percent of subjects with clinically important change in drug-induced liver injury (Safety population)
End point description: A clinically important change in drug-induced liver injury is defined as a change (from baseline) in alanine aminotransferase (ALT) greater than 3 times the upper limit of normal (ULN) or a change in total bilirubin greater than 2 times ULN, that is confirmed upon repeat measurement.	
End point type	Primary
End point timeframe: From baseline (before 1st infusion) to Day 29	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	415	416	413	
Units: Percent of subjects				
number (not applicable)	1	0.5	0	

Statistical analyses

Statistical analysis title	Non-inferiority assessment CSL112 (2 g) vs Placebo
Comparison groups	CSL112 (2 g) v Placebo
Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	= 0.1241
Method	Newcombe-Wilson score method
Parameter estimate	Difference in event rates (%)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	2.5

Notes:

[1] - The upper limit of the confidence interval for the difference in rates (2.5%) is less than the non-inferiority limit of 4%. Therefore, the non-inferiority criterion was satisfied.

Statistical analysis title	Non-inferiority assessment CSL112 (6 g) vs Placebo
Comparison groups	CSL112 (6 g) v Placebo
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
P-value	= 0.4994
Method	Newcombe-Wilson score method
Parameter estimate	Difference in event rates (%)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.7

Notes:

[2] - The upper limit of the confidence interval for the difference in rates (1.7%) is less than the non-inferiority limit of 4%. Therefore, the non-inferiority criterion was satisfied.

Primary: Percent of subjects with clinically important change in renal status (Safety population)

End point title	Percent of subjects with clinically important change in renal status (Safety population)
End point description: A clinically important change in renal status is defined as a serum creatinine (Cr) increase to $\geq 1.5 \times$ the baseline value that is confirmed upon repeat measurement.	
End point type	Primary
End point timeframe: From baseline (before 1st infusion) to Day 29	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	415	416	413	
Units: Percent of subjects				
number (not applicable)	0	0.7	0.2	

Statistical analyses

Statistical analysis title	Non-inferiority assessment CSL112 (2 g) vs Placebo
Comparison groups	CSL112 (2 g) v Placebo
Number of subjects included in analysis	828
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[3]
P-value	= 0.4988
Method	Newcombe-Wilson score method
Parameter estimate	Difference in event rates (%)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.7

Notes:

[3] - The upper limit of the confidence interval for the difference in rates (0.7%) is less than the non-inferiority limit of 5%. Therefore, the non-inferiority criterion was satisfied.

Statistical analysis title	Non-inferiority assessment CSL112 (6 g) vs Placebo
Comparison groups	CSL112 (6 g) v Placebo
Number of subjects included in analysis	829
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[4]
P-value	= 0.6241
Method	Newcombe-Wilson score method
Parameter estimate	Difference in event rates (%)
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.9

Notes:

[4] - The upper limit of the confidence interval for the difference in rates (1.9%) is less than the non-inferiority limit of 5%. Therefore, the non-inferiority criterion was satisfied.

Secondary: Time-to-first occurrence of a major adverse cardiovascular event (MACE) (ITT population)

End point title	Time-to-first occurrence of a major adverse cardiovascular event (MACE) (ITT population)
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End point description:

The MACE composite secondary endpoint was a 4-component composite comprised of the time to the first of the following events: CV death, nonfatal myocardial infarction, ischemic stroke (non-hemorrhagic), and hospitalization for unstable angina. The percentage of subjects with time-to-first occurrence of a major adverse cardiovascular event (MACE) are presented.

End point type	Secondary
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End point timeframe:

From the start of the first infusion up to approximately 382 days

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	419	421	418	
Units: Percent of subjects				
number (not applicable)	6.4	5.7	5.5	

Statistical analyses

Statistical analysis title	CSL112 (2 g)
Comparison groups	CSL112 (2 g) v Placebo
Number of subjects included in analysis	837
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5733 ^[5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.05

Notes:

[5] - Stratified log-rank p-value

Statistical analysis title	CSL112 (6 g)
Comparison groups	CSL112 (6 g) v Placebo
Number of subjects included in analysis	839
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9717 ^[6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.8

Notes:

[6] - Stratified log-rank p-value

Secondary: Baseline-Corrected Plasma Concentrations of Apolipoprotein A-I (apoA-I) and Phosphatidylcholine (PC) at End of Infusion 1 for all subjects (PK population)

End point title	Baseline-Corrected Plasma Concentrations of Apolipoprotein A-I (apoA-I) and Phosphatidylcholine (PC) at End of Infusion 1 for all subjects (PK population)
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End point description:

Apolipoprotein A-I (apoA-I) and Phosphatidylcholine (PC) are analytes of CSL112

End point type	Secondary
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End point timeframe:

Before infusion 1 and end of Infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	396	404	403	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	35.9 (± 22.13)	136.1 (± 54.37)	-4.7 (± 13.46)	
PC	57.7 (± 31.12)	180.4 (± 74.4)	-1.2 (± 20.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 4 for all subjects (PK population)

End point title	Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 4 for all subjects (PK population)
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End point description:

apoA-I and PC are analytes of CSL112

End point type	Secondary
End point timeframe:	
Before infusion 1 and end of Infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	366	370	370	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	52.1 (± 55.03)	158 (± 55.07)	5.4 (± 26.47)	
PC	48.7 (± 55.75)	186.8 (± 79.39)	-12.9 (± 42.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 1 for subjects with normal renal function (PK population)

End point title	Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 1 for subjects with normal renal function (PK population)
End point description:	
apoA-I and PC are analytes of CSL112	
End point type	Secondary
End point timeframe:	
Before infusion 1 and end of Infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	175	183	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	36 (± 25.35)	134.5 (± 48.25)	-4 (± 16.95)	
PC	58 (± 37.06)	177.4 (± 67.93)	-1.3 (± 25.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 4 for subjects with normal renal function (PK population)

End point title	Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 4 for subjects with normal renal function (PK population)
End point description: apoA-I and PC are analytes of CSL112	
End point type	Secondary
End point timeframe: Before infusion 1 and end of Infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	173	160	171	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	54.7 (± 74.94)	154.3 (± 53.64)	4.8 (± 28.19)	
PC	47.6 (± 64.67)	182 (± 80.74)	-12.3 (± 44.89)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 1 for subjects with mild renal impairment (PK population)

End point title	Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 1 for subjects with mild renal impairment (PK population)
End point description: apoA-I and PC are analytes of CSL112	
End point type	Secondary
End point timeframe: Before infusion 1 and end of Infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	189	212	203	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	35.9 (± 19.05)	135.5 (± 59.05)	-5.3 (± 9.7)	
PC	57.8 (± 24.71)	180.6 (± 79.5)	-0.8 (± 14.95)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 4 for subjects with mild renal impairment (PK population)

End point title	Baseline-Corrected Plasma Concentrations of apoA-I and PC at End of Infusion 4 for subjects with mild renal impairment (PK population)
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End point description:

apoA-I and PC are analytes of CSL112

End point type	Secondary
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End point timeframe:

Before infusion 1 and end of Infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	171	195	183	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	49.3 (± 26.73)	158.4 (± 56.19)	6 (± 25.68)	
PC	50.6 (± 47.17)	188.3 (± 79.39)	-13.2 (± 40.08)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
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End point description:

Cmax is the maximal plasma concentration.

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	21	18	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	42.6 (± 11.2)	147.4 (± 31.9)	7.1 (± 7.9)	
PC	67.7 (± 19.2)	196.4 (± 36.2)	11.1 (± 15.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
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End point description:

Cmax is the maximal plasma concentration.

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	19	17	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	57.6 (± 19.5)	164.3 (± 33.4)	12.7 (± 19.5)	
PC	59 (± 34.2)	187.4 (± 49.9)	9.1 (± 43.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
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End point description:

Cmax is the maximal plasma concentration.

End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	10	13	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	40.9 (± 12)	135.1 (± 22.8)	7.8 (± 8.3)	
PC	61.9 (± 21)	184.9 (± 31.5)	13 (± 16.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
End point description:	
Cmax is the maximal plasma concentration.	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	8	12	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	60.8 (± 19.2)	149 (± 26.9)	17.5 (± 20.3)	
PC	45.8 (± 26.4)	176.1 (± 54)	20.1 (± 44.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
End point description: Cmax is the maximal plasma concentration.	
End point type	Secondary
End point timeframe: Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	5	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	44.6 (± 10.2)	160.7 (± 37)	5.2 (± 7.3)	
PC	74.6 (± 14.7)	211.3 (± 37.5)	6 (± 10.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Cmax for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
End point description: Cmax is the maximal plasma concentration.	
End point type	Secondary
End point timeframe: Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	5	
Units: mg/dL				
arithmetic mean (standard deviation)				
apoA-I	53.7 (± 20.1)	169.7 (± 29.3)	1 (± 12.1)	
PC	74.8 (± 37)	190.4 (± 46.7)	-17.4 (± 28.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Tmax for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Plasma Tmax for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
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End point description:

Tmax is time to maximal plasma concentration

End point type	Secondary
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End point timeframe:

Before and for 7 days after the first infusion

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	21	18	
Units: hours				
median (full range (min-max))				
apoA-I	2.23 (1.7 to 236.9)	2.17 (2 to 4)	46.8 (0 to 216.3)	
PC	2.23 (1.7 to 8.4)	2.17 (2 to 4)	5.29 (0 to 188.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Tmax for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Plasma Tmax for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
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End point description:

Tmax is time to maximal plasma concentration

End point type	Secondary
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End point timeframe:

Before and for 7 days after the fourth infusion

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	19	17	
Units: hours				
median (full range (min-max))				
apoA-I	2.13 (2 to 23.5)	2.25 (2 to 4.2)	119 (0 to 332.9)	
PC	2.17 (2 to 53.1)	2.25 (2 to 4.2)	46.93 (0 to 187.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Tmax for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Plasma Tmax for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
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End point description:

Tmax is time to maximal plasma concentration

End point type	Secondary
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End point timeframe:

Before and for 7 days after the first infusion

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	10	13	
Units: hours				
median (full range (min-max))				
apoA-I	2.25 (1.7 to 236.9)	2.17 (2 to 3.4)	96.1 (0 to 216.3)	
PC	2.22 (1.7 to 8.4)	2.17 (2 to 3.4)	8.1 (0 to 188.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Tmax for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Plasma Tmax for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
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End point description:

Tmax is time to maximal plasma concentration

End point type	Secondary
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End point timeframe:

Before and for 7 days after the fourth infusion

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	8	12	
Units: hours				
median (full range (min-max))				
apoA-I	2.13 (2.1 to 3.5)	2.17 (2 to 2.4)	119.3 (0 to 332.9)	
PC	2.17 (2.1 to 53.1)	2.17 (2 to 2.4)	29 (0 to 187.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Tmax for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Plasma Tmax for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
End point description:	
Tmax is time to maximal plasma concentration	
End point type	Secondary
End point timeframe:	
Before and for 7 days after the first infusion	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	5	
Units: hours				
median (full range (min-max))				
apoA-I	2.18 (2.1 to 3.4)	2.22 (2.1 to 4)	0 (0 to 117.9)	
PC	2.28 (2.1 to 5)	2.22 (2.1 to 4)	0 (0 to 5.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Tmax for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Plasma Tmax for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
End point description:	
Tmax is time to maximal plasma concentration	
End point type	Secondary

End point timeframe:

Before and for 7 days after the fourth infusion

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	5	
Units: hours				
median (full range (min-max))				
apoA-I	2.17 (2 to 23.5)	2.25 (2.1 to 4.2)	72.5 (0 to 166.5)	
PC	2.17 (2 to 8)	2.25 (2.1 to 4.2)	48.3 (9 to 166.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma area under the curve (AUC) AUC0 - last for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma area under the curve (AUC) AUC0 - last for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
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End point description:

Area under the plasma concentration time curve (AUC) from time point zero (baseline) to the last quantifiable time-point before the analyte first returns to baseline [AUC0 - last]

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24	21	18	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	1703 (± 2149)	4819 (± 2580)	-766 (± 2248)	
PC	-66.12 (± 3653)	869 (± 3796)	-2096 (± 3372)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
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End point description:

Area under the plasma concentration time curve (AUC) from time point zero (baseline) to the last quantifiable time-point before the analyte first returns to baseline [AUC0 - last]

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	19	17	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	4579 (± 2705)	8985 (± 4263)	747 (± 3226)	
PC	70.7 (± 5327)	2499 (± 7662)	-2185 (± 5189)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
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End point description:

Area under the plasma concentration time curve (AUC) from time point zero (baseline) to the last quantifiable time-point before the analyte first returns to baseline [AUC0 - last]

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	10	13	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	1278 (± 1742)	3762 (± 2367)	-516 (± 2091)	
PC	-1382 (± 2853)	-137 (± 4057)	-1337 (± 2590)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
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End point description:

Area under the plasma concentration time curve (AUC) from time point zero (baseline) to the last quantifiable time-point before the analyte first returns to baseline [AUC0 - last]

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	8	12	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	4513 (± 2701)	8609 (± 4500)	1632 (± 3235)	
PC	-2130 (± 4691)	3609 (± 10232)	-542 (± 4480)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
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End point description:

Area under the plasma concentration time curve (AUC) from time point zero (baseline) to the last quantifiable time-point before the analyte first returns to baseline [AUC0 - last]

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	10	5	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	2205 (± 2543)	5917 (± 2568)	-1416 (± 2763)	
PC	1489 (± 4003)	1828 (± 3661)	-4068 (± 4634)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma AUC0 - last for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
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End point description:

Area under the plasma concentration time curve (AUC) from time point zero (baseline) to the last quantifiable time-point before the analyte first returns to baseline [AUC0 - last]

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	10	5	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	4659 (± 2854)	8786 (± 4201)	-1376 (± 2205)	
PC	2712 (± 5010)	1541 (± 5815)	-6128 (± 4998)	

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
End point description: AUC from baseline to time point t (AUC0-t)	
End point type	Secondary
End point timeframe: Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	24 ^[7]	21 ^[8]	18 ^[9]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I (0-24h)	496 (± 212)	1929 (± 557)	-168 (± 158)	
apoA-I (0-48h)	731 (± 447)	2903 (± 944)	-331 (± 375)	
apoA-I (0-72h)	880 (± 726)	3516 (± 1248)	-439 (± 632)	
apoA-I (0-96h)	1006 (± 1104)	3943 (± 1581)	-541 (± 940)	
apoA-I (0-168h)	1009 (± 1761)	4734 (± 2382)	-452 (± 1498)	
PC (0-24h)	508 (± 349)	1545 (± 552)	-92 (± 229)	
PC (0-48h)	466 (± 744)	1627 (± 872)	-315 (± 522)	
PC (0-72h)	418 (± 1251)	1713 (± 1209)	-549 (± 886)	
PC (0-96h)	389 (± 1841)	1712 (± 1694)	-780 (± 1346)	
PC (0-168h)	-405 (± 3636)	1273 (± 2764)	-1494 (± 2501)	

Notes:

[7] - apoA-I (0-168h, n=16);

PC (0-96h, n=23);

PC (0-168h, n=16)

[8] - apoA-I (0-96h, n=20);

apoA-I (0-168h, n=20);

PC (0-168h, n=15)

[9] - apoA-I (0-168h, n=10);

PC (0-168h, n=11)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
End point description: AUC from baseline to time point t (AUC0-t)	
End point type	Secondary
End point timeframe: Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22 ^[10]	19 ^[11]	17 ^[12]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I (0-24h)	881 (± 422)	2392 (± 655)	-57 (± 377)	
apoA-I (0-48h)	1593 (± 798)	3913 (± 1235)	-55 (± 759)	
apoA-I (0-72h)	2195 (± 1177)	5050 (± 1794)	-6 (± 1160)	
apoA-I (0-96h)	2741 (± 1526)	6000 (± 2292)	90 (± 1590)	
apoA-I (0-168h)	3997 (± 2655)	8865 (± 3200)	1635 (± 3540)	
PC (0-24h)	462 (± 681)	1564 (± 1051)	-488 (± 772)	
PC (0-48h)	472 (± 1293)	1765 (± 1948)	-902 (± 1433)	
PC (0-72h)	509 (± 1989)	1899 (± 2823)	-1173 (± 2168)	
PC (0-96h)	518 (± 2679)	1951 (± 3681)	-1417 (± 2894)	
PC (0-168h)	-625 (± 4963)	2655 (± 6024)	-442 (± 6319)	

Notes:

[10] - apoA-I (0-168h, n=18);

PC (0-168h, n=16)

[11] - apoA-I (0-168h, n=16);

PC (0-168h, n=16)

[12] - apoA-I (0-168h, n=8);

PC (0-168h, n=8)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
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End point description:

AUC from baseline to time point t (AUC0-t)

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13 ^[13]	10 ^[14]	13 ^[15]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I (0-24h)	418 (± 117)	1653 (± 496)	-149 (± 123)	
apoA-I (0-48h)	547 (± 204)	2521 (± 955)	-316 (± 332)	
apoA-I (0-72h)	628 (± 337)	3064 (± 1280)	-435 (± 579)	
apoA-I (0-96h)	692 (± 554)	3342 (± 1642)	-528 (± 883)	
apoA-I (0-168h)	821 (± 1387)	3780 (± 2353)	-275 (± 1461)	
PC (0-24h)	364 (± 245)	1347 (± 661)	-46 (± 160)	

PC (0-48h)	145 (± 536)	1294 (± 1025)	-235 (± 441)	
PC (0-72h)	-38 (± 946)	1325 (± 1421)	-426 (± 759)	
PC (0-96h)	-256 (± 1415)	1218 (± 2005)	-569 (± 1162)	
PC (0-168h)	-1511 (± 3053)	437 (± 2061)	-1089 (± 2188)	

Notes:

[13] - apoA-I (0-168h, n=8);
PC (0-168h, n=9)

[14] - apoA-I (0-96h, n=9);
apoA-I (0-168h, n=9);
PC (0-168h, n=7)

[15] - apoA-I (0-168h, n=7);
PC (0-168h, n=7)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
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End point description:

AUC from baseline to time point t (AUC0-t)

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12 ^[16]	8 ^[17]	12 ^[18]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I (0-24h)	929 (± 396)	2098 (± 463)	20 (± 417)	
apoA-I (0-48h)	1668 (± 753)	3459 (± 1001)	105 (± 820)	
apoA-I (0-72h)	2252 (± 1116)	4497 (± 1478)	249 (± 1232)	
apoA-I (0-96h)	2769 (± 1473)	5360 (± 1909)	459 (± 1666)	
apoA-I (0-168h)	3811 (± 2706)	8342 (± 2549)	2486 (± 2804)	
PC (0-24h)	189 (± 483)	1524 (± 1388)	-295 (± 819)	
PC (0-48h)	-59 (± 952)	1796 (± 2613)	-523 (± 1446)	
PC (0-72h)	-306 (± 1544)	2000 (± 3773)	-605 (± 2133)	
PC (0-96h)	-573 (± 2204)	2078 (± 4905)	-633 (± 2772)	
PC (0-168h)	-3853 (± 3242)	4584 (± 7822)	1253 (± 4446)	

Notes:

[16] - apoA-I (0-168h, n=10);
PC (0-168h, n=8)

[17] - apoA-I (0-168h, n=6);
PC (0-168h, n=6)

[18] - apoA-I (0-168h, n=7);
PC (0-168h, n=7)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
End point description:	
AUC from baseline to time point t (AUC0-t)	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11 ^[19]	10 ^[20]	5 ^[21]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I (0-24h)	589 (± 263)	2219 (± 515)	-218 (± 238)	
apoA-I (0-48h)	949 (± 560)	3308 (± 847)	-370 (± 514)	
apoA-I (0-72h)	1179 (± 946)	3998 (± 1152)	-451 (± 834)	
apoA-I (0-96h)	1376 (± 1468)	4517 (± 1465)	-576 (± 1188)	
apoA-I (0-168h)	1196 (± 2155)	5624 (± 2293)	-865 (± 1824)	
PC (0-24h)	678 (± 386)	1777 (± 353)	-212 (± 348)	
PC (0-48h)	845 (± 797)	1968 (± 623)	-523 (± 705)	
PC (0-72h)	956 (± 1393)	2093 (± 950)	-871 (± 1196)	
PC (0-96h)	1227 (± 2058)	2194 (± 1351)	-1329 (± 1769)	
PC (0-168h)	1018 (± 4052)	2004 (± 3214)	2203 (± 3197)	

Notes:

[19] - apoA-I (0-168h, n=8);

PC (0-96h, n=10);

PC (0-168h, n=7)

[20] - PC (0-168h, n=8)

[21] - apoA-I (0-168h, n=3);

PC (0-168h, n=4)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma AUC0-t for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
End point description:	
AUC from baseline to time point t (AUC0-t)	
End point type	Secondary

End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10 ^[22]	10 ^[23]	5 ^[24]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I (0-24h)	823 (± 466)	2469 (± 573)	-243 (± 170)	
apoA-I (0-48h)	1503 (± 881)	4049 (± 1221)	-440 (± 436)	
apoA-I (0-72h)	2128 (± 1304)	5226 (± 1910)	-617 (± 741)	
apoA-I (0-96h)	2707 (± 1669)	6212 (± 2503)	-796 (± 1045)	
apoA-I (0-168h)	4229 (± 2754)	8840 (± 3678)	-4322 (± 0)	
PC (0-24h)	789 (± 760)	1518 (± 799)	-950 (± 405)	
PC (0-48h)	1110 (± 1402)	1650 (± 1474)	-1810 (± 1001)	
PC (0-72h)	1487 (± 2090)	1726 (± 2176)	-2536 (± 1731)	
PC (0-96h)	1826 (± 2706)	1751 (± 2867)	-3297 (± 2471)	
PC (0-168h)	2603 (± 4295)	1316 (± 4998)	-12308 (± 0)	

Notes:

[22] - apoA-I (0-168h, n=8);

PC (0-168h, n=8)

[23] - apoA-I (0-168h, n=9);

PC (0-168h, n=9)

[24] - apoA-I (0-168h, n=1);

PC (0-168h, n=1)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
End point description:	
AUC0-∞ is plasma area under the curve (AUC0-infinity)	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	16 ^[25]	1 ^[26]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	1425 (± 1297)	6090 (± 3642)	0 (± 0)	
PC	1850 (± 3120)	1678 (± 651)	6979 (± 0)	

Notes:

[25] - PC (n=10)

[26] - apoA-I (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
End point description:	
AUC0-∞ is plasma area under the curve (AUC0-infinity)	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10 ^[27]	15 ^[28]	1 ^[29]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	15540 (± 19437)	13570 (± 6965)	4615 (± 0)	
PC	2015 (± 2855)	12863 (± 16731)	0 (± 0)	

Notes:

[27] - PC (n=6)

[28] - PC (n=11)

[29] - PC (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
End point description:	
AUC0-∞ is plasma area under the curve (AUC0-infinity)	

End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[30]	8 ^[31]	0 ^[32]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	589 (± 17)	4505 (± 2528)	()	
PC	490 (± 1540)	1596 (± 785)	()	

Notes:

[30] - apoA-I (n=2)

[31] - PC (n=5)

[32] - No values collected for this point.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
End point description:	
AUC0-∞ is plasma area under the curve (AUC0-infinity)	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7 ^[33]	5 ^[34]	1 ^[35]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	17079 (± 23224)	12422 (± 7399)	4615 (± 0)	
PC	638 (± 566)	16142 (± 17777)	0 (± 0)	

Notes:

[33] - PC (n=4)

[34] - PC (n=3)

[35] - PC (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
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End point description:

AUC0-∞ is plasma area under the curve (AUC0-infinity)

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4 ^[36]	7 ^[37]	1 ^[38]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	1842 (± 1451)	8032 (± 4220)	0 (± 0)	
PC	3210 (± 4052)	1761 (± 566)	6979 (± 0)	

Notes:

[36] - PC (n=3)

[37] - PC (n=5)

[38] - apoA-I (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma AUC0-∞ for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
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End point description:

AUC0-∞ is plasma area under the curve (AUC0-infinity)

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[39]	9 ^[40]	0 ^[41]	
Units: mg•h/dL				
arithmetic mean (standard deviation)				
apoA-I	11951 (± 7374)	13157 (± 6734)	()	

PC	4769 (\pm 4128)	12827 (\pm 18453)	()	
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Notes:

[39] - PC (n=2)

[40] - PC (n=7)

[41] - Values were not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Terminal Half-life (t1/2) for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma Terminal Half-life (t1/2) for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	16 ^[42]	1 ^[43]	
Units: hours				
arithmetic mean (standard deviation)				
apoA-I	46.4 (\pm 33.1)	53.9 (\pm 38.7)	0 (\pm 0)	
PC	32.9 (\pm 29.6)	9.7 (\pm 7.2)	241.2 (\pm 0)	

Notes:

[42] - PC (n=10)

[43] - apoA-I (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Terminal Half-life (t1/2) for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma Terminal Half-life (t1/2) for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10 ^[44]	15 ^[45]	1 ^[46]	
Units: hours				
arithmetic mean (standard deviation)				
apoA-I	269.1 (± 292)	103.6 (± 61.1)	145 (± 0)	
PC	21.5 (± 20.6)	156.3 (± 245.8)	0 (± 0)	

Notes:

[44] - PC (n=6)

[45] - PC (n=11)

[46] - PC (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Terminal Half-life (t_{1/2}) for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Terminal Half-life (t _{1/2}) for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[47]	8 ^[48]	0 ^[49]	
Units: hours				
arithmetic mean (standard deviation)				
apoA-I	7.5 (± 1.7)	41.4 (± 24.1)	()	
PC	34 (± 27.7)	12.3 (± 8.9)	()	

Notes:

[47] - apoA-I (n=2)

[48] - PC (n=5)

[49] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Terminal Half-life (t_{1/2}) for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Terminal Half-life (t _{1/2}) for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7 ^[50]	5 ^[51]	1 ^[52]	
Units: hours				
arithmetic mean (standard deviation)				
apoA-I	271.6 (± 317.4)	96.5 (± 47.3)	145 (± 0)	
PC	9.1 (± 9.3)	121.1 (± 102.7)	0 (± 0)	

Notes:

[50] - PC (n=4)

[51] - PC (n=3)

[52] - PC (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Terminal Half-life (t_{1/2}) for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Terminal Half-life (t _{1/2}) for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4 ^[53]	7 ^[54]	1 ^[55]	
Units: hours				
arithmetic mean (standard deviation)				
apoA-I	65.9 (± 17.5)	66.4 (± 51.4)	0 (± 0)	
PC	31.8 (± 37.7)	7.1 (± 4.4)	241.2 (± 0)	

Notes:

[53] - PC (n=3)

[54] - PC (n=5)

[55] - apoA-I (n=0)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Terminal Half-life (t_{1/2}) for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Terminal Half-life (t _{1/2}) for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[56]	9 ^[57]	0 ^[58]	
Units: hours				
arithmetic mean (standard deviation)				
apoA-I	263.1 (± 285.4)	99.2 (± 68.2)	()	
PC	46.3 (± 2.2)	185.6 (± 306.5)	()	

Notes:

[56] - PC (n=2)

[57] - PC (n=7)

[58] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[59]	16 ^[60]	0 ^[61]	
Units: L/h				
arithmetic mean (standard deviation)				
apoA-I	0.29 (± 0.27)	0.15 (± 0.13)	()	
PC	0.32 (± 0.26)	0.61 (± 0.26)	()	

Notes:

[59] - PC (n=5)

[60] - PC (n=10)

[61] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
End point description:	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17 ^[62]	16 ^[63]	0 ^[64]	
Units: L/h				
arithmetic mean (standard deviation)				
apoA-I	0.09 (± 0.1)	0.07 (± 0.02)	()	
PC	0.11 (± 0.09)	0.57 (± 1.12)	()	

Notes:

[62] - PC (n=6)

[63] - PC (n=11)

[64] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
End point description:	
End point type	Secondary

End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	8 ^[65]	0 ^[66]	
Units: L/h				
arithmetic mean (standard deviation)				
apoA-I	0.33 (± 0.01)	0.19 (± 0.17)	()	
PC	0.41 (± 0.38)	0.68 (± 0.35)	()	

Notes:

[65] - PC (n=5)

[66] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10 ^[67]	6 ^[68]	0 ^[69]	
Units: L/h				
arithmetic mean (standard deviation)				
apoA-I	0.11 (± 0.12)	0.08 (± 0.02)	()	
PC	0.24 (± 0)	0.19 (± 0.12)	()	

Notes:

[67] - PC (n=1)

[68] - PC (n=5)

[69] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
End point description:	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4 ^[70]	7 ^[71]	0 ^[72]	
Units: L/h				
arithmetic mean (standard deviation)				
apoA-I	0.27 (± 0.35)	0.09 (± 0.05)	()	
PC	0.26 (± 0.23)	0.54 (± 0.13)	()	

Notes:

[70] - PC (n=3)

[71] - PC (n=5)

[72] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Clearance (CL) for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
End point description:	
End point type	Secondary
End point timeframe:	
Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4	

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7 ^[73]	9 ^[74]	0 ^[75]	
Units: L/h				
arithmetic mean (standard deviation)				
apoA-I	0.05 (± 0.02)	0.08 (± 0.03)	()	
PC	0.08 (± 0.07)	1.01 (± 1.63)	()	

Notes:

[73] - PC (n=5)

[74] - PC (n=5)

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma volume of distribution at steady state (Vss) for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma volume of distribution at steady state (Vss) for apoA-I and PC after Infusion 1 for all subjects (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6 ^[76]	16 ^[77]	0 ^[78]	
Units: Liters				
arithmetic mean (standard deviation)				
apoA-I	33.4 (± 64.7)	7.4 (± 3.1)	()	
PC	6.1 (± 4.4)	14.4 (± 33.3)	()	

Notes:

[76] - PC (n=5)

[77] - PC (n=10)

[78] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Vss for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)

End point title	Baseline-corrected plasma Vss for apoA-I and PC after Infusion 4 for all subjects (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10 ^[79]	15 ^[80]	0 ^[81]	
Units: Liters				
arithmetic mean (standard deviation)				
apoA-I	18.7 (± 16.6)	9.4 (± 4.7)	()	
PC	10.7 (± 7.5)	58.3 (± 94.9)	()	

Notes:

[79] - PC (n=6)

[80] - PC (n=11)

[81] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Vss for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Vss for apoA-I and PC after Infusion 1 for subjects with normal renal function (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	8 ^[82]	0 ^[83]	
Units: Liters				
arithmetic mean (standard deviation)				
apoA-I	3.8 (± 0.9)	8.1 (± 3.8)	()	
PC	8.3 (± 7.7)	24.7 (± 47.2)	()	

Notes:

[82] - PC (n=5)

[83] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Vss for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)

End point title	Baseline-corrected plasma Vss for apoA-I and PC after Infusion 4 for subjects with normal renal function (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7 ^[84]	5 ^[85]	0 ^[86]	
Units: Liters				
arithmetic mean (standard deviation)				
apoA-I	18.7 (± 16.1)	9.4 (± 2.5)	()	
PC	11.4 (± 8.3)	17 (± 10.3)	()	

Notes:

[84] - PC (n=4)

[85] - PC (n=3)

[86] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Vss for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Vss for apoA-I and PC after Infusion 1 for subjects with mild renal impairment (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 1

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4 ^[87]	7 ^[88]	0 ^[89]	
Units: Liters				
arithmetic mean (standard deviation)				
apoA-I	48.2 (± 78.1)	6.4 (± 2.3)	()	
PC	4.7 (± 1.3)	4 (± 1.5)	()	

Notes:

[87] - PC (n=3)

[88] - PC (n=5)

[89] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline-corrected plasma Vss for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)

End point title	Baseline-corrected plasma Vss for apoA-I and PC after Infusion 4 for subjects with mild renal impairment (PK/PD population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1 (baseline) and for up to approximately 7 days after infusion 4

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3 ^[90]	9 ^[91]	0 ^[92]	
Units: Liters				
arithmetic mean (standard deviation)				
apoA-I	18.7 (± 21.3)	9.4 (± 5.9)	()	
PC	9.3 (± 8.2)	83.1 (± 114)	()	

Notes:

[90] - PC (n=2)

[91] - PC (n=7)

[92] - Values not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of subjects with the occurrence of adverse drug reactions (Safety population)

End point title	Percent of subjects with the occurrence of adverse drug reactions (Safety population)
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End point description:

The overall percentage of subjects:

- with adverse events (AEs), including local tolerability events, that begin during or within 1 hour of an infusion; or
- with AEs considered to be causally related to the test product; or
- who experience an AE for which the incidence rate in an active treatment arm exceeds the exposure-adjusted incidence rate in the placebo arm by 30% or more, provided the difference in incidence rates is 1% or more

End point type	Secondary
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End point timeframe:

From the start of infusion 1, up to approximately Day 382

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	415	416	413	
Units: percent of subjects				
number (not applicable)	31.8	28.4	23.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of subjects with any AE (Safety population)

End point title	Percent of subjects with any AE (Safety population)
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End point description:

End point type	Secondary
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End point timeframe:

From the start of infusion 1, up to approximately Day 382

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	415	416	413	
Units: Percent of subjects				
number (not applicable)	50.6	51.4	49.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of subjects who experience bleeding events (Safety population)

End point title	Percent of subjects who experience bleeding events (Safety population)
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End point description:

Percent of subjects who experience bleeding events as defined by the Bleeding Academic Research Consortium (BARC) criteria (Mehran et al, 2011)

End point type	Secondary
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End point timeframe:

From the start of infusion 1, up to approximately Day 112

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	415	416	413	
Units: Percent of subjects				
number (not applicable)	9.2	9.1	12.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to end of study in serum antibodies to CSL112 and apoA-I (Safety population)

End point title	Change from baseline to end of study in serum antibodies to CSL112 and apoA-I (Safety population)
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End point description:

End point type	Secondary
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End point timeframe:

Before infusion 1, up to approximately Day 112

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	377	389	380	
Units: Titer				
arithmetic mean (standard deviation)				
Anti-CSL112 antibody	0 (± 0.14)	0 (± 0.2)	0 (± 0.2)	
Anti-apoA-I antibody	0 (± 0.09)	0 (± 0.14)	0 (± 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with positive serology results for IgG and IgM antibodies to parvovirus B19 (Serology population)

End point title	Number of subjects with positive serology results for IgG and IgM antibodies to parvovirus B19 (Serology population)
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End point description:

Assessments (i.e., evidence of seroconversion or infection) will be conducted for parvovirus B19.

End point type	Secondary
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End point timeframe:

Study Day 112

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	60	60	
Units: Number of subjects				
number (not applicable)				
IgG	40	48	44	
IgM	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with parvovirus B19 DNA in serum (Serology population)

End point title	Number of subjects with parvovirus B19 DNA in serum (Serology population)
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End point description:

Assessments (i.e., evidence of seroconversion or infection) will be conducted for parvovirus B19

End point type	Secondary
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End point timeframe:

Study Day 112

End point values	CSL112 (2 g)	CSL112 (6 g)	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	60	60	60	
Units: Number of subjects				
number (not applicable)				
Not detected	57	60	59	
< 101 IU/mL	1	0	1	
Missing	2	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

1 year, 10 months

Adverse event reporting additional description:

The Serious Adverse Events include both treatment-emergent and non-treatment emergent events.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Safety Lead-in [CSL112 (2 g)]
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Reporting group description:

In the safety lead-in, a small number of subjects (evenly stratified between subjects with normal renal function or mild renal impairment) were administered a single, 2 g infusion of CSL112.

Reporting group title	CSL112 (2 g)
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Reporting group description:

CSL112 (low dose) was administered as an intravenous (IV) infusion once weekly for 4 consecutive weeks.

Reporting group title	CSL112 (6 g)
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Reporting group description:

CSL112 (high dose) was administered as an IV infusion once weekly for 4 consecutive weeks.

Reporting group title	Placebo
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Reporting group description:

Placebo was administered as an IV infusion at the same frequency, volume and duration as either the low dose or high dose CSL112 infusion.

Serious adverse events	Safety Lead-in [CSL112 (2 g)]	CSL112 (2 g)	CSL112 (6 g)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	66 / 415 (15.90%)	54 / 416 (12.98%)
number of deaths (all causes)	1	5	4
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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

Colon cancer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock haemorrhagic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Arterial haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Hypertensive crisis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Peripheral artery occlusion			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 9 (0.00%)	9 / 415 (2.17%)	4 / 416 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 9 (0.00%)	2 / 415 (0.48%)	4 / 416 (0.96%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Vascular stent restenosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Vascular stent thrombosis			

subjects affected / exposed	1 / 9 (11.11%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 9 (11.11%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 9 (0.00%)	2 / 415 (0.48%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Dyspnoea exertional			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Pneumothorax			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Pulmonary fibrosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Pharyngeal oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)	2 / 415 (0.48%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed mood			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Mental disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Contusion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Coronary artery restenosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Fall			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pubis fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Femoral neck fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Subdural haematoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 9 (0.00%)	5 / 415 (1.20%)	6 / 416 (1.44%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 9 (0.00%)	6 / 415 (1.45%)	3 / 416 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	3 / 415 (0.72%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 9 (0.00%)	3 / 415 (0.72%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	3 / 416 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ventricular tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	3 / 415 (0.72%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 9 (0.00%)	2 / 415 (0.48%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute coronary syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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 aneurysm			

subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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 arrest			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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 asthma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Intracardiac thrombus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Palpitations			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prinzmetal angina			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			

subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Ventricular fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Ventricular septal defect acquired			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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 failure acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Cardiomyopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Coronary artery dissection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Coronary artery occlusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Supraventricular tachycardia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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 failure			
subjects affected / exposed	1 / 9 (11.11%)	3 / 415 (0.72%)	3 / 416 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	2 / 415 (0.48%)	2 / 416 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia			
subjects affected / exposed	0 / 9 (0.00%)	3 / 415 (0.72%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal ganglia haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Carotid artery disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic neuropathy			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Cluster headache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Presyncope			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Blood and lymphatic system disorders			
Iron deficiency anaemia			

subjects affected / exposed	0 / 9 (0.00%)	2 / 415 (0.48%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic anaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
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			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	2 / 416 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 415 (0.48%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Abdominal pain upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
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 gastritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Crohn's disease			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Pancreatitis acute			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Retroperitoneal haematoma			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Vomiting			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Pancreatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Cholestasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Angioedema			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Postrenal failure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Musculoskeletal pain			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fasciitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Polymyalgia rheumatica			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Haematoma infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Oral fungal infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Septic shock			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 415 (0.24%)	0 / 416 (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
Nasopharyngitis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Postoperative abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Soft tissue infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Urosepsis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	0 / 416 (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
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 415 (0.00%)	1 / 416 (0.24%)
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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	55 / 413 (13.32%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal neoplasm			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder neoplasm			

subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon cancer			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arterial haemorrhage			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			

subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral artery occlusion			
subjects affected / exposed	2 / 413 (0.48%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	5 / 413 (1.21%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	4 / 413 (0.97%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular stent restenosis			

subjects affected / exposed	2 / 413 (0.48%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Vascular stent thrombosis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea exertional			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleurisy			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary fibrosis			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngeal oedema			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety			

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depressed mood			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mental disorder			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery restenosis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Fall			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pubis fracture			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	5 / 413 (1.21%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		

Angina unstable				
subjects affected / exposed	4 / 413 (0.97%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 413 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	1 / 413 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	1 / 413 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	2 / 413 (0.48%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute coronary syndrome				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial tachycardia				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac aneurysm			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac asthma			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracardiac thrombus			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial ischaemia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prinzmetal angina			

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus bradycardia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular fibrillation			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular septal defect acquired			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiomyopathy			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery dissection			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery occlusion			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mitral valve incompetence			

subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Carotid artery stenosis			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal ganglia haemorrhage			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Carotid artery disease			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			

subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic neuropathy				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxic-ischaemic encephalopathy				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar radiculopathy				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	1 / 413 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cluster headache				
subjects affected / exposed	1 / 413 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 413 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Presyncope				

subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic anaemia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual impairment			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic gastritis			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mechanical ileus			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal haematoma			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			

subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholestasis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postrenal failure			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc disorder			

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fasciitis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Polymyalgia rheumatica			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridial infection			

subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematoma infection				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oral fungal infection				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 413 (0.48%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 413 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				

subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nasopharyngitis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative abscess			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 413 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety Lead-in [CSL112 (2 g)]	CSL112 (2 g)	CSL112 (6 g)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)	15 / 415 (3.61%)	23 / 416 (5.53%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 9 (11.11%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences (all)	1	0	0
Extrasystoles			
subjects affected / exposed	1 / 9 (11.11%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 9 (11.11%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	15 / 415 (3.61%)	23 / 416 (5.53%)
occurrences (all)	0	19	24
Skin and subcutaneous tissue disorders			
Skin exfoliation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 415 (0.00%)	0 / 416 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 413 (2.18%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 413 (0.00%)		
occurrences (all)	0		

Extrasystoles subjects affected / exposed occurrences (all)	0 / 413 (0.00%) 0		
Nervous system disorders Syncope subjects affected / exposed occurrences (all)	0 / 413 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all)	9 / 413 (2.18%) 10		
Skin and subcutaneous tissue disorders Skin exfoliation subjects affected / exposed occurrences (all)	0 / 413 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2013	<ol style="list-style-type: none">1. A safety lead-in period was added to assess the safety and tolerability of CSL112 compared to placebo in subjects with acute myocardial infarction, with the requirement of safety data review by the Data Safety Monitoring Board from this lead-in period prior to enrolment of subjects into the main study. The safety lead-in period was added to this study to fulfill a request from FDA.2. A pharmacokinetic (PK)/pharmacodynamics (PD) substudy was added to the protocol with intense sampling to occur in approximately 48 subjects after doses 1 and 4, with only sparse PK/PD sampling of subjects to be included in the main study.3. New assessments were added to schedules for monitoring safety:<ol style="list-style-type: none">i. presence of hypovolemiaii. determination and review of serum creatinine and ALT values prior to dosingiii. drug hypersensitivity reactionsiv. urinalysisv. exploratory renal biomarkers (limited to PK/PD substudy only).4. The objectives of the study were modified and changes were made to the corresponding endpoints. The secondary objectives now include characterization of the safety and tolerability and the pharmacokinetics of CSL112 in subjects with acute myocardial infarction.5. The inclusion criterion defining eligibility restrictions for subjects who undergo angiography were modified, reducing the magnitude of allowable increases in serum creatinine post contrast agent administration. Further definition was also provided regarding the meaning of "significant" ST/T wave changes.6. Modifications/clarifications of and additional dose delay/dose stopping rules were added to the protocol with respect to confirming subject eligibility for initial and subsequent investigational product treatment based on serum creatinine values.
01 October 2014	<ol style="list-style-type: none">1. Assessment of bilirubin was included in criteria for determining stable hepatic function and levels were defined for dose delay/stopping rules in the main study.2. Serology and nucleic acid testing was revised to test only for the presence of parvovirus B19 instead of testing for 5 pathogens (ie, HIV 1/2, hepatitis A virus, hepatitis B virus, hepatitis C virus, and parvovirus B19) as originally planned.3. Inclusion of a new methods section and requirement of additional measurements (repeat assessment of hemoglobin level, serum haptoglobin levels, lactate dehydrogenase, total and direct bilirubin levels, including the calculation of indirect bilirubin, and urine hemosiderin) for assessment of hemolysis for any ≥ 2 g/dL decrease in hemoglobin not explained by overt blood loss.4. Parameters were set for the maximum duration between infusions (at least 7 days and no more than 10 days) and allowance for fewer than 4 infusions to be administered if the total duration from Study Day 1 would exceed 30 days (ie, discussed in text as "missed infusions").5. Drug-related adverse events (adverse reactions), changing the time window relative to infusion from within 72 hours to within 1 hour for classification and reporting requirements of adverse drug reactions that occur with an incidence $> 30\%$ of that of the placebo rate and that occur in at least 1% of subjects is redefined.

14 July 2015	<ol style="list-style-type: none"> 1. Allowed for screening and randomization to occur on the same day if specific criteria are met. 2. For screening and randomization occurring on the same day, allowed for a single blood draw to be performed at screening to collect two samples, one for local and one for central laboratory testing. 3. Decreased retention time for virology samples to 1 year from 5 years. 4. Further defined adverse events of special interest and added potential Hy's law and drug hypersensitivity reactions to the adverse event of special interest section. 5. Further defined the drug hypersensitivity reaction assessment. 6. Added collection of a standard of care serum creatinine value prior to administration of contrast agent. 7. Modified the secondary endpoint language for evaluation of adverse drug reactions. 8. Added the definition of first medical contact 9. In reviewing the available study data and the FDA-suggested guidelines and analyses for early dosing of investigational product following contrast administration, the DSMB assessed the safety of the investigational product when administered within 48 h from contrast administration and determined that earlier treatment could be initiated in the US cohort of patients. <p>The recommendation harmonized the US with all other sites and allowed the study to be conducted under a single global harmonized protocol (allowing administration of investigational product to be as early as 12 h after the index event or 12 h after the administration of IV contrast media once renal function is determined to be stable).</p>
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study was not designed to test for efficacy and was underpowered to assess efficacy. The overall number of MACE was low and the number of subjects with complete follow-up through 1 year was also low (89 of 1258 subjects; 7.1%).

Notes: