Clinical trial results:
An Open-Label, Single-Arm, Multicenter Pilot Study to Evaluate Safety, Tolerability, and Efficacy of ALN-PCSSC in Subjects with Homozygous Familial Hypercholesterolemia

Summary

EudraCT number	2016-003376-49
Trial protocol	NL
Global end of trial date	08 October 2018

Results information

Result version number	v1 (current)
This version publication date	16 November 2019
First version publication date	16 November 2019

Trial information

Trial identification

Sponsor protocol code	MDCO-PCS-16-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02963311
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	The Medicines Company
Sponsor organisation address	8 Sylvan Way, Parsippany, United States, NJ 07054
Public contact	Global Health Science Center, The Medicines Company, +1 9732906000, medical.information@themedco.com
Scientific contact	Global Health Science Center, The Medicines Company, +1 9732906000, medical.information@themedco.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	08 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the effect of 90 and 180 days of subcutaneous ALN-PCSSC (inclisiaran) on the percentage change from Day 1 in low-density lipoprotein cholesterol (LDL-C) in subjects with homozygous familial hypercholesterolemia.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and in compliance with Good Clinical Practice (GCP) for protection of subjects, as required by the applicable governmental regulations, directives, and guidelines in operation at the time of the study.

The study protocol and amendments and informed consent form (ICF) were reviewed and approved by the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) at each participating site.

Prior to initiation of any study-related procedures, the nature of the study was fully explained to all subjects and the ICF was signed by the subject. Consent was captured on an ICF form approved by the IEC/IRB and included the elements required by the International Conference on Harmonization and GCP guidelines.

Background therapy:

Subjects taking part in this clinical study received guideline recommended standard of care as background therapy (including maximally-tolerated statin therapy and/or other LDL-C lowering therapies) when administered inclisiran.

Evidence for comparator:

N/A

Actual start date of recruitment	13 December 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	South Africa: 3
Worldwide total number of subjects	4
EEA total number of subjects	1

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)	4
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Not applicable

Pre-assignment

Screening details:

Subjects enrolled must have a bodyweight of 40 kg or greater. Subjects were excluded if they had low density lipoprotein (LDL) or plasma apheresis within 8 weeks prior to the screening visit, used Mipomersen or Lomitapide therapy within 5 months or had previous treatment with monoclonal antibodies directed towards PCSK9 within 8 weeks of screening.

Pre-assignment period milestones

Number of subjects started	9[1]
Number of subjects completed	4

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Physician decision: 4

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Nine subjects were screened; four subjects failed screening and five were consented into the study. One subject withdrew consent prior to treatment. Therefore, four subjects were treated with inclisiran.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Single arm

Arm description:

A Phase II, open label, single-arm, multicenter pilot study designed to test the efficacy and duration of effect of inclisiran sodium 300 mg in subjects with Homozygous Familial Hypercholesterolemia (HoFH).

Arm type	Experimental
Investigational medicinal product name	Inclisiran
Investigational medicinal product code	ALN-60212
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mg/ml

Number of subjects in period 1	Single arm
Started	4
Completed	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	4	4	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	37.0		
standard deviation	± 13.04	-	
Gender categorical Units: Subjects			
Female	2	2	
Male	2	2	

End points

End points reporting groups

Reporting group title	Single arm

Reporting group description:

A Phase II, open label, single-arm, multicenter pilot study designed to test the efficacy and duration of effect of inclisiran sodium 300 mg in subjects with Homozygous Familial Hypercholesterolemia (HoFH).

Primary: Percentage change from Day 1 to Day 90 in LDL-C

End point title	Percentage change from Day 1 to Day 90 in LDL-C[1]

End point description:

300 milligrams (mg) administered subcutaneous (SC) on Day 1. Participants with a mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Primary

End point timeframe:

Day 1, Day 90

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the small number of subjects, and the fact that the data are not normally distributed, the data are presented as descriptive statistics with no inferential and limited summary statistics presented.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percent change				
arithmetic mean (confidence interval 95%)	-12.26 (-43.75 to 19.24)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage Change From Day 1 to Day 180 (or Final Visit) in LDL-C

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in LDL-C[2]

End point description:

300 milligrams (mg) administered subcutaneous (SC) on Day 1. Participants with a mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-

cholesterol (LDL-C)-lowering therapies

End point type	Primary

End point timeframe:

Day 1 to Day 180

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the small number of subjects, and the fact that the data are not normally distributed, the data are presented as descriptive statistics with no inferential and limited summary statistics presented.

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percent change				
arithmetic mean (confidence interval 95%)	-20.96 (-49.97 to 8.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in LDL-C

End point title	Absolute Change From Day 1 to Day 90 in LDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-56.3 (± 115.18)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in LDL-C

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in LDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180 (or Final Visit)

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-105.3 (± 116.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 60 in PCSK9

End point title	Percentage Change From Day 1 to Day 60 in PCSK9

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 60

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percentage				
arithmetic mean (standard deviation)	-64.9 (± 18.33)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in PCSK9

End point title	Percentage Change From Day 1 to Day 90 in PCSK9

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percentage				
arithmetic mean (standard deviation)	-59.0 (± 16.46)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 60 in PCSK9

End point title	Absolute Change From Day 1 to Day 60 in PCSK9

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.

Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 60

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng/mL				
arithmetic mean (standard deviation)	-654.1 (± 564.67)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in PCSK9

End point title	Absolute Change From Day 1 to Day 90 in PCSK9

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: ng/mL				
arithmetic mean (standard deviation)	602.3 (± 559.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in Total Cholesterol

End point title	Percentage Change From Day 1 to Day 90 in Total Cholesterol

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percent change				
arithmetic mean (standard deviation)	-13.9 (± 14.84)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in Total Cholesterol

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in Total Cholesterol

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180 (or final visit)

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: percent change				
arithmetic mean (standard deviation)	-19.8 (± 13.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in Total Cholesterol

End point title	Absolute Change From Day 1 to Day 90 in Total Cholesterol

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	77.8 (± 103.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in Total Cholesterol

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in Total Cholesterol

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-118.0 (± 103.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in Triglycerides

End point title	Percentage Change From Day 1 to Day 90 in Triglycerides

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percent change				
arithmetic mean (standard deviation)	-21.0 (± 30.99)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in Triglycerides

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in Triglycerides

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	11.67 (± 20.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in Triglycerides

End point title	Absolute Change From Day 1 to Day 90 in Triglycerides

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a

second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-35.5 (± 38.76)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 Day 180 (or Final Visit) in Triglycerides

End point title	Absolute Change From Day 1 Day 180 (or Final Visit) in Triglycerides

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-26.3 (± 24.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in HDL-C

End point title	Percentage Change From Day 1 to Day 90 in HDL-C

End point description:

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-12.1 (± 17.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in HDL-C

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in HDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-19.8 (± 11.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in HDL-C

End point title	Absolute Change From Day 1 to Day 90 in HDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-6.0 (± 9.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in HDL-C

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in HDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-9.5 (± 4.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in Non-HDL-C

End point title	Percentage Change From Day 1 to Day 90 in Non-HDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-13.9 (± 14.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in Non-HDL-C

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in Non-HDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-19.7 (± 13.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in Non-HDL-C

End point title	Absolute Change From Day 1 to Day 90 in Non-HDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit.

Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-71.8 (± 97.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in Non-HDL-C

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in Non-HDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-108.5 (± 99.38)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in VLDL-C

End point title	Percentage Change From Day 1 to Day 90 in VLDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	8.5 (± 65.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in VLDL-C

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in VLDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	55.5 (± 131.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in VLDL-C

End point title	Absolute Change From Day 1 to Day 90 in VLDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-15.5 (± 28.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in VLDL-C

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in VLDL-C

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-3.3 (± 37.32)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in Apolipoprotein A1

End point title	Percentage Change From Day 1 to Day 90 in Apolipoprotein A1

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-8.3 (± 12.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein A1

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein A1

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-14.2 (± 14.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in Apolipoprotein A1

End point title	Absolute Change From Day 1 to Day 90 in Apolipoprotein A1

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a

second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-11.5 (± 17.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein A1

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein A1

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-19.8 (± 19.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in Apolipoprotein B

End point title	Percentage Change From Day 1 to Day 90 in Apolipoprotein B

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-26.6 (± 14.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein B

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein B

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is

given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary
End point timeframe:	
Day 1 to Day 180	

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-25.0 (± 14.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in Apolipoprotein B

End point title	Absolute Change From Day 1 to Day 90 in Apolipoprotein B

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary
End point timeframe:	
Day 1 to Day 90	

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-95.3 (± 78.16)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein B

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in Apolipoprotein B

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 180

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-86.3 (± 72.02)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 90 in Lipoprotein-a

End point title	Percentage Change From Day 1 to Day 90 in Lipoprotein-a

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.

Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary
End point timeframe:	
Day 1 to Day 90	

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-3.5 (± 15.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Day 1 to Day 180 (or Final Visit) in Lipoprotein-a

End point title	Percentage Change From Day 1 to Day 180 (or Final Visit) in Lipoprotein-a

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary
End point timeframe:	
Day 1 to Day 180	

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage change				
arithmetic mean (standard deviation)	-11.8 (± 15.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 90 in Lipoprotein-a

End point title	Absolute Change From Day 1 to Day 90 in Lipoprotein-a

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.
Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary

End point timeframe:

Day 1 to Day 90

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	13.5 (± 21.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute Change From Day 1 to Day 180 (or Final Visit) in Lipoprotein-a

End point title	Absolute Change From Day 1 to Day 180 (or Final Visit) in Lipoprotein-a

End point description:

All subjects received open label inclisiran on Day 1. The dosing interval was determined by PCSK9 level at Day 60 or 90 or rate of change of PCSK9 levels between Days 60 and 90. If a second dose of study drug was deemed necessary (if mean serum proprotein convertase subtilisin/kexin type 9 (PCSK9) levels not suppressed by >70% at Day 60 or Day 90, as compared to baseline, subjects will receive a second dose at Day 90 or Day 104, respectively, based on PCSK9 levels from the previous visit. Participants also received standard of care as background therapy.
Inclisiran: Inclisiran is a small interfering ribonucleic acid (siRNA) that inhibits PCSK9 synthesis and is given as SC injections.

Standard of Care: Included maximally-tolerated statin therapy and/or other low density lipoprotein-cholesterol (LDL-C)-lowering therapies.

End point type	Secondary
End point timeframe:	
Day 1 to Day 180	

End point values	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: mg/dL				
arithmetic mean (standard deviation)	-23.8 (± 52.73)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 18 months	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups	
Reporting group title	Inclisiran

Reporting group description: -

Serious adverse events	Inclisiran		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Inclisiran		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)		
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Road traffic accident			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Cardiac disorders			

Angina unstable subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1 1 / 4 (25.00%) 1		
Infections and infestations Cystitis			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2016	Amend 01
18 August 2017	Amendment 2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported