Clinical trial results:
Two part (double-blind inclisiran versus placebo [Year 1] followed by open-label inclisiran [Year 2]) randomized multicenter study to evaluate safety, tolerability, and efficacy of inclisiran in adolescents (12 to less than 18 years) with heterozygous familial hypercholesterolemia and elevated LDL-cholesterol (ORION-16)

Summary

EudraCT number	2020-002757-18
Trial protocol	HU NO DE SI NL GR FR IT PL HR SK CZ
Global end of trial date	27 November 2024

Results information

Result version number	v1 (current)
This version publication date	07 June 2025
First version publication date	07 June 2025

Trial information

Trial identification

Sponsor protocol code	CKJX839C12301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04652726
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002214-PIP01-17
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 November 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the efficacy, safety and tolerability of inclisiran in adolescents (aged 12 to <18 years) with heterozygous familial hypercholesterolaemia (HeFH).

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 January 2021
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	Brazil: 10
Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Jordan: 5
Country: Number of subjects enrolled	Lebanon: 3
Country: Number of subjects enrolled	Malaysia: 1
Country: Number of subjects enrolled	Netherlands: 25
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Poland: 5
Country: Number of subjects enrolled	Russian Federation: 3

Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Slovenia: 1
Country: Number of subjects enrolled	South Africa: 7
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Türkiye: 7
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	141
EEA total number of subjects	75

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)	141
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were randomized from 51 study centers:ARG (1), BRA (3), CAN (1), CZE (2), FRA (3), DEU (2), GRC (1), HUN (1), ISR (2), ITA (4), JOR (1), LBN (1), MYS (1), NLD (2), NOR (1), POL (2), RUS (2), SVK (1), SVN (1), ZAF (3), ESP(4), CHE (1), TWN (1), TUR (4), GBR (1), USA (5)

Pre-assignment

Screening details:

The study had an approximately 4-week screening/run-in period

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1- Inclisiran

Arm description:

Inclisiran sodium 300 mg subcutaneous (sc) injection (given at Days 1, 90 and 270)

Arm type	Experimental
Investigational medicinal product name	Inclisiran
Investigational medicinal product code	KJX839
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Inclisiran sodium 300mg(equivalent to 284mginclisiran) in 1.5 mL solution

Arm title	Part 1 - Placebo

Arm description:

Placebo sc injection (given at Day 1, 90 and 270)

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

Dosage and administration details:

Placebo formulation to the active drug formulation

Number of subjects in period 1	Part 1- Inclisiran	Part 1 - Placebo
Started	93	48
Completed	91	48
Not completed	2	0
Physician decision	1	-
Participant/guardian decision	1	-

Period 2	
Period 2 title	Part 2 (Open-label period)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part 2 – Inclisiran (Total)

Arm description:

Inclisiran sodium 300 mg sc injection (given at Days 450 and 630). In addition, participants assigned to placebo in Part 1 received inclisiran sodium 300 mg sc injection on Day 360, while participants assigned to inclisiran in Part 1 received placebo sc injection on Day 360

Arm type	Experimental
Investigational medicinal product name	Inclisiran
Investigational medicinal product code	KJX839
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Inclisiran sodium 300mg(equivalent to 284mginclisiran) in 1.5 mLsolution

Number of subjects in period 2	Part 2 – Inclisiran (Total)
Started	139
Completed	139

Baseline characteristics

Reporting groups	
Reporting group title	Part 1- Inclisiran
Reporting group description:	
Inclisiran sodium 300 mg subcutaneous (sc) injection (given at Days 1, 90 and 270)	
Reporting group title	Part 1 - Placebo
Reporting group description:	
Placebo sc injection (given at Day 1, 90 and 270)	

Reporting group values	Part 1- Inclisiran	Part 1 - Placebo	Total
Number of subjects	93	48	141
Age Categorical Units: participants			
<=18 years	93	48	141
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Age Continuous Units: years			
arithmetic mean	15.2	14.9	
standard deviation	± 2.02	± 1.80	-
Sex: Female, Male Units: participants			
Female	51	24	75
Male	42	24	66
Race/Ethnicity, Customized Units: Subjects			
Asian	4	0	4
Black or African American	5	0	5
Other	4	0	4
White	80	48	128

End points

End points reporting groups	
Reporting group title	Part 1- Inclisiran
Reporting group description:	
Inclisiran sodium 300 mg subcutaneous (sc) injection (given at Days 1, 90 and 270)	
Reporting group title	Part 1 - Placebo
Reporting group description:	
Placebo sc injection (given at Day 1, 90 and 270)	
Reporting group title	Part 2 – Inclisiran (Total)
Reporting group description:	
Inclisiran sodium 300 mg sc injection (given at Days 450 and 630). In addition, participants assigned to placebo in Part 1 received inclisiran sodium 300 mg sc injection on Day 360, while participants assigned to inclisiran in Part 1 received placebo sc injection on Day 360	

Primary: Percentage change in LDL-C from baseline to Day 330 (Part 1/Year 1)	
End point title	Percentage change in LDL-C from baseline to Day 330 (Part 1/Year 1)
End point description:	
Percentage change in low-density lipoprotein cholesterol (LDL-C) from baseline to Day 330 (Year 1)	
End point type	Primary
End point timeframe:	
Baseline and Day 330	

End point values	Part 1- Inclisiran	Part 1 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	48		
Units: percent change in LDL-C				
least squares mean (confidence interval 95%)	-27.14 (-32.04 to -22.24)	1.40 (-3.97 to 6.78)		

Statistical analyses

Statistical analysis title	Difference between Inclisiran and Placebo
Comparison groups	Part 1- Inclisiran v Part 1 - Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-28.54

Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.81
upper limit	-21.27

Secondary: Time-adjusted percent change in LDL-C from baseline after Day 90 and up to Day 330 (Part 1/Year 1)

End point title	Time-adjusted percent change in LDL-C from baseline after Day 90 and up to Day 330 (Part 1/Year 1)

End point description:

Time-adjusted percent change in LDL-C (after Day 90 and up to Day 330), calculated as the average of percent changes from baseline to Days 150, 270 and 330

End point type	Secondary

End point timeframe:

Baseline, after Day 90 up to Day 330

End point values	Part 1- Inclisiran	Part 1 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	48		
Units: Time-adjusted percent change in LDL-C				
least squares mean (confidence interval 95%)	-26.04 (-30.11 to -21.98)	3.26 (-2.37 to 8.89)		

Statistical analyses

Statistical analysis title	Difference between Inclisiran and Placebo
Comparison groups	Part 1- Inclisiran v Part 1 - Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	MMRM
Parameter estimate	LS Mean
Point estimate	-29.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.24
upper limit	-22.36

Secondary: Percent change in non-HDL-C from baseline up to Day 330 (Part 1/Year 1)

End point title	Percent change in non-HDL-C from baseline up to Day 330 (Part 1/Year 1)
End point description:	
Percentage change in non-high density lipoprotein cholesterol (non-HDL-C) from baseline to Day 330.	
End point type	Secondary
End point timeframe:	
Baseline and Day 330	

End point values	Part 1- Inclisiran	Part 1 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	48		
Units: Percent change in non-HDL-C				
least squares mean (confidence interval 95%)	-25.04 (-29.68 to -20.41)	1.76 (-3.25 to 6.77)		

Statistical analyses

Statistical analysis title	Difference between Inclisiran and Placebo
Comparison groups	Part 1- Inclisiran v Part 1 - Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-26.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.63
upper limit	-19.97

Secondary: Percent change in Lp(a) from baseline up to Day 330 (Part 1/Year 1)

End point title	Percent change in Lp(a) from baseline up to Day 330 (Part 1/Year 1)
End point description:	
Percentage change in lipoprotein (a) [Lp(a)] from baseline to Day 330.	
End point type	Secondary
End point timeframe:	
Baseline and Day 330	

End point values	Part 1- Inclisiran	Part 1 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	48		
Units: Percent change in Lp(a)				
least squares mean (confidence interval 95%)	-5.04 (-14.21 to 4.13)	1.14 (-5.48 to 7.77)		

Statistical analyses

Statistical analysis title	Difference between Inclisiran and Placebo
Comparison groups	Part 1- Inclisiran v Part 1 - Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1419
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-6.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.48
upper limit	5.12

Secondary: Percent change in Apo B from baseline up to Day 330 (Part 1/Year 1)

End point title	Percent change in Apo B from baseline up to Day 330 (Part 1/Year 1)
End point description:	
Percentage change in apolipoprotein B (Apo B) from baseline to Day 330.	
End point type	Secondary
End point timeframe:	
Baseline and Day 330	

End point values	Part 1- Inclisiran	Part 1 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	48		
Units: Percent change in Apo B				
least squares mean (confidence interval 95%)	-21.46 (-25.59 to -17.33)	4.24 (-0.07 to 8.56)		

Statistical analyses

Statistical analysis title	Difference between Inclisiran and Placebo
Comparison groups	Part 1- Inclisiran v Part 1 - Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-25.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.68
upper limit	-19.73

Secondary: Absolute change in LDL-C from baseline to up Day 330 (Part 1/Year 1)

End point title	Absolute change in LDL-C from baseline to up Day 330 (Part 1/Year 1)
End point description:	
Absolute change in LDL-C from baseline to Day 330.	
End point type	Secondary
End point timeframe:	
Baseline and Day 330	

End point values	Part 1- Inclisiran	Part 1 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	48		
Units: mg/dL				
least squares mean (confidence interval 95%)	-50.54 (-59.22 to -41.86)	-0.55 (-10.48 to 9.38)		

Statistical analyses

Statistical analysis title	Difference between Inclisiran and Placebo
Comparison groups	Part 1- Inclisiran v Part 1 - Placebo

Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-49.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.18
upper limit	-36.81

Secondary: Percent change in total cholesterol from baseline up to Day 330 (Part 1/Year 1)

End point title	Percent change in total cholesterol from baseline up to Day 330 (Part 1/Year 1)
End point description:	
Percentage change in total cholesterol from baseline to Day 330.	
End point type	Secondary
End point timeframe:	
Baseline and Day 330	

End point values	Part 1- Inclisiran	Part 1 - Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	48		
Units: Percent change in total cholesterol				
least squares mean (confidence interval 95%)	-18.72 (-22.48 to -14.96)	0.48 (-3.46 to 4.42)		

Statistical analyses

Statistical analysis title	Difference between Inclisiran and Placebo
Comparison groups	Part 1- Inclisiran v Part 1 - Placebo
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean
Point estimate	-19.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.65
upper limit	-13.75

Secondary: Percent change in LDL-C from baseline up to Day 720

End point title	Percent change in LDL-C from baseline up to Day 720

End point description:

Percentage change in LDL-C from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	139	48	
Units: Percent change in LDL-C				
arithmetic mean (standard deviation)				
DAY 90 (n=93,48,0)	-23.9 (± 22.14)	999 (± 999)	-0.1 (± 20.16)	
DAY 150 (n=92,48,0)	-32.5 (± 21.47)	999 (± 999)	6.4 (± 28.83)	
DAY 270 (n=92,48,0)	-19.0 (± 28.31)	999 (± 999)	2.1 (± 22.44)	
DAY 330 (n=90,48,0)	-27.8 (± 22.95)	999 (± 999)	1.5 (± 20.59)	
DAY 360 (n=90,48,0)	-26.1 (± 22.71)	999 (± 999)	1.5 (± 30.56)	
DAY 450 (n=0,0,139)	999 (± 999)	-24.5 (± 26.45)	999 (± 999)	
DAY 510 (n=0,0,139)	999 (± 999)	-32.5 (± 22.80)	999 (± 999)	
DAY 630 (n=0,0,139)	999 (± 999)	-26.5 (± 24.33)	999 (± 999)	
Day 720 (study completion) (n=0,0,139)	999 (± 999)	-33.7 (± 23.98)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in LDL-C from baseline up to Day 720

End point title	Absolute change in LDL-C from baseline up to Day 720

End point description:

Absolute change in LDL-C from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 90 (n=93,48,0)	-45.4 (± 45.26)	999 (± 999)	-3.0 (± 35.02)	
DAY 150 (n=92,48,0)	-61.0 (± 45.84)	999 (± 999)	6.6 (± 46.22)	
DAY 270 (n=92,48,0)	-38.4 (± 55.77)	999 (± 999)	1.0 (± 36.92)	
DAY 330 (n=90,48,0)	-51.9 (± 45.47)	999 (± 999)	-0.3 (± 38.04)	
DAY 360 (n=90,48,0)	-49.0 (± 44.49)	999 (± 999)	-2.9 (± 51.74)	
DAY 450 (n=0,0,139)	999 (± 999)	-46.3 (± 52.51)	999 (± 999)	
DAY 510 (n=0,0,139)	999 (± 999)	-60.8 (± 48.88)	999 (± 999)	
DAY 630 (n=0,0,139)	999 (± 999)	-50.9 (± 50.30)	999 (± 999)	
Day 720 (study completion) (n=0,0,139)	999 (± 999)	-64.1 (± 53.91)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Apo B from baseline up to Day 720

End point title	Percent change in Apo B from baseline up to Day 720

End point description:

Percentage change in apolipoprotein B (Apo B) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in Apo B				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-25.1 (± 18.18)	999 (± 999)	2.2 (± 20.77)	
DAY 330 (n=90, 48, 0)	-21.9 (± 19.51)	999 (± 999)	3.9 (± 18.13)	
DAY 360 (n=90, 48, 0)	-19.3 (± 21.36)	999 (± 999)	1.7 (± 22.70)	
DAY 510 (n=0, 0, 138)	999 (± 999)	-24.5 (± 21.77)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-25.7 (± 21.71)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in Apo B from baseline up to Day 720

End point title	Absolute change in Apo B from baseline up to Day 720
End point description:	
Absolute change in apolipoprotein B (Apo B) from baseline to each assessment time up to Day 720.	
End point type	Secondary
End point timeframe:	
Baseline, up to Day 720	

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-33.3 (± 28.20)	999 (± 999)	0.0 (± 27.38)	
DAY 330 (n=90, 48, 0)	-29.2 (± 28.04)	999 (± 999)	2.9 (± 23.47)	
DAY 360 (n=90, 48, 0)	-26.1 (± 29.59)	999 (± 999)	-0.6 (± 28.72)	
DAY 510 (n=0, 0, 138)	999 (± 999)	-33.5 (± 32.13)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-35.4 (± 33.83)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Lp(a) from baseline up to Day 720

End point title	Percent change in Lp(a) from baseline up to Day 720

End point description:

Percentage change in lipoprotein (a) [Lp(a)] from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in Lp(a)				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-13.4 (± 22.60)	999 (± 999)	5.4 (± 23.96)	
DAY 330 (n=90, 48, 0)	-7.2 (± 30.80)	999 (± 999)	1.1 (± 24.25)	
DAY 360 (n=90, 48, 0)	-9.3 (± 28.44)	999 (± 999)	3.6 (± 23.27)	
DAY 510 (n=0, 0, 139)	999 (± 999)	-13.3 (± 28.81)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-4.2 (± 163.74)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in Lp(a) from baseline up to Day 720

End point title	Absolute change in Lp(a) from baseline up to Day 720

End point description:

Absolute change in lipoprotein (a) [Lp(a)] from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: nmol/L				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-12.5 (± 34.73)	999 (± 999)	3.2 (± 20.67)	
DAY 330 (n=90, 48, 0)	-9.5 (± 33.81)	999 (± 999)	5.3 (± 21.55)	
DAY 360 (n=90, 48, 0)	-10.2 (± 31.16)	999 (± 999)	4.4 (± 22.99)	
DAY 510 (n=0, 0, 139)	999 (± 999)	-10.1 (± 34.98)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-9.0 (± 50.08)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in non-HDL-C from baseline up to Day 720

End point title	Percent change in non-HDL-C from baseline up to Day 720

End point description:

Percentage change in non-high density lipoprotein cholesterol (non-HDL-C) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in non-HDL-C				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-29.0 (± 20.15)	999 (± 999)	5.1 (± 24.85)	
DAY 330 (n=90, 48, 0)	-25.7 (± 21.69)	999 (± 999)	1.8 (± 19.43)	
DAY 360 (n=90, 48, 0)	-24.0 (± 21.74)	999 (± 999)	1.2 (± 27.43)	
DAY 510 (n=0, 0, 139)	999 (± 999)	-29.9 (± 21.60)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-31.0 (± 23.04)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in non-HDL-C from baseline up to Day 720

End point title	Absolute change in non-HDL-C from baseline up to Day 720

End point description:

Absolute change in non-high density lipoprotein cholesterol (non-HDL-C) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-60.2 (± 47.41)	999 (± 999)	5.7 (± 47.61)	
DAY 330 (n=90, 48, 0)	-52.6 (± 46.93)	999 (± 999)	0.5 (± 39.20)	
DAY 360 (n=90, 48, 0)	-49.7 (± 46.30)	999 (± 999)	-3.0 (± 52.75)	
DAY 510 (n=0, 0, 139)	999 (± 999)	-62.0 (± 51.09)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-65.1 (± 56.16)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in total cholesterol from baseline up to Day 720

End point title	Percent change in total cholesterol from baseline up to Day 720

End point description:

Percentage change in total cholesterol from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in total cholesterol				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-22.6 (± 15.77)	999 (± 999)	4.4 (± 20.49)	
DAY 330 (n=90, 48, 0)	-19.2 (± 17.77)	999 (± 999)	0.6 (± 15.46)	
DAY 360 (n=90, 48, 0)	-18.5 (± 17.18)	999 (± 999)	0.6 (± 21.81)	
DAY 510 (n=0, 0, 139)	999 (± 999)	-23.0 (± 17.50)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-23.7 (± 18.29)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in total cholesterol from baseline up to Day 720

End point title	Absolute change in total cholesterol from baseline up to Day 720

End point description:

Absolute change in total cholesterol from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	-59.0 (± 47.79)	999 (± 999)	6.6 (± 48.08)	
DAY 330 (n=90, 48, 0)	-49.4 (± 47.77)	999 (± 999)	-0.9 (± 38.48)	
DAY 360 (n=90, 48, 0)	-48.2 (± 47.06)	999 (± 999)	-3.1 (± 52.66)	
DAY 510 (n=0, 0, 139)	999 (± 999)	-59.6 (± 51.06)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-62.3 (± 55.05)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in triglycerides from baseline up to Day 720

End point title	Percent change in triglycerides from baseline up to Day 720

End point description:

Percentage change in triglycerides from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in triglycerides				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	16.2 (± 78.18)	999 (± 999)	2.8 (± 37.44)	
DAY 330 (n=90, 48, 0)	1.8 (± 38.39)	999 (± 999)	9.7 (± 43.04)	
DAY 360 (n=90, 48, 0)	1.7 (± 40.03)	999 (± 999)	3.8 (± 35.76)	
DAY 510 (n=0, 0, 139)	999 (± 999)	3.4 (± 43.08)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	1.9 (± 41.84)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in triglycerides from baseline up to Day 720

End point title	Absolute change in triglycerides from baseline up to Day 720

End point description:

Absolute change in triglycerides from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 150 (n= 92, 48, 0)	6.9 (± 64.67)	999 (± 999)	-4.8 (± 31.53)	
DAY 330 (n= 90, 48, 0)	-2.9 (± 35.01)	999 (± 999)	3.5 (± 35.55)	
DAY 360 (n= 90, 48, 0)	-3.1 (± 38.13)	999 (± 999)	-1.7 (± 28.47)	
DAY 510 (n= 0, 0, 139)	999 (± 999)	-4.2 (± 34.70)	999 (± 999)	
Day 720 (study completion) (n= 0, 0, 139)	999 (± 999)	-4.8 (± 36.21)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in HDL-C from baseline up to Day 720

End point title	Percent change in HDL-C from baseline up to Day 720

End point description:

Percentage change in high density lipoprotein cholesterol (HDL-C) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in HDL-C				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	3.6 (± 18.88)	999 (± 999)	3.6 (± 16.49)	
DAY 330 (n=90, 48, 0)	7.4 (± 19.15)	999 (± 999)	-1.9 (± 16.15)	
DAY 360 (n=90, 48, 0)	4.4 (± 19.54)	999 (± 999)	0.9 (± 12.39)	
DAY 510 (n=0, 0, 139)	999 (± 999)	6.6 (± 19.84)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	7.4 (± 20.40)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in HDL-C from baseline up to Day 720

End point title	Absolute change in HDL-C from baseline up to Day 720
End point description:	
Absolute change in high density lipoprotein cholesterol (HDL-C) from baseline to each assessment time up to Day 720.	
End point type	Secondary
End point timeframe:	
Baseline, up to Day 720	

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	1.2 (± 10.23)	999 (± 999)	0.9 (± 8.07)	
DAY 330 (n=90, 48, 0)	3.2 (± 9.57)	999 (± 999)	-1.4 (± 7.77)	
DAY 360 (n=90, 48, 0)	1.5 (± 9.59)	999 (± 999)	-0.1 (± 6.23)	
DAY 510 (n=0, 0, 139)	999 (± 999)	2.4 (± 9.32)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	2.8 (± 9.75)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in VLDL-C from baseline up to Day 720

End point title	Percent change in VLDL-C from baseline up to Day 720
End point description:	
Percentage change in very low density lipoprotein cholesterol (VLDL-C) from baseline to each assessment time up to Day 720.	
End point type	Secondary
End point timeframe:	
Baseline, up to Day 720	

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in VLDL-C				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	11.8 (± 60.04)	999 (± 999)	3.3 (± 38.25)	
DAY 330 (n=90, 48, 0)	0.6 (± 39.00)	999 (± 999)	10.0 (± 42.29)	
DAY 360 (n=90, 48, 0)	1.0 (± 40.15)	999 (± 999)	4.7 (± 35.65)	
DAY 510 (n=0, 0, 139)	999 (± 999)	1.4 (± 41.13)	999 (± 999)	

Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	1.9 (± 42.20)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolut change in VLDL-C from baseline up to Day 720

End point title	Absolut change in VLDL-C from baseline up to Day 720

End point description:

Absolute change in very low density lipoprotein cholesterol (VLDL-C) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	0.7 (± 10.02)	999 (± 999)	-0.9 (± 6.37)	
DAY 330 (n=90, 48, 0)	-0.7 (± 7.04)	999 (± 999)	0.8 (± 7.07)	
DAY 360 (n=90, 48, 0)	-0.7 (± 7.63)	999 (± 999)	-0.2 (± 5.66)	
DAY 510 (n=0, 0, 139)	999 (± 999)	-1.2 (± 6.90)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	-1.0 (± 7.40)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in Apo A1 from baseline up to Day 720

End point title	Absolute change in Apo A1 from baseline up to Day 720

End point description:

Absolute change in apolipoprotein A1 (Apo A1) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: mg/dL				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	3.3 (± 21.76)	999 (± 999)	0.0 (± 17.72)	
DAY 330 (n=90, 48, 0)	6.1 (± 21.16)	999 (± 999)	-2.8 (± 14.24)	
DAY 360 (n=90, 48, 0)	2.7 (± 21.87)	999 (± 999)	-2.6 (± 13.89)	
DAY 510 (n=0, 0, 138)	999 (± 999)	7.5 (± 22.24)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	5.4 (± 21.61)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Apo A1 from baseline up to Day 720

End point title	Percent change in Apo A1 from baseline up to Day 720

End point description:

Percentage change in apolipoprotein A1 (Apo A1) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	139	48	
Units: Percent change in Apo A1				
arithmetic mean (standard deviation)				
DAY 150 (n=92, 48, 0)	3.7 (± 15.40)	999 (± 999)	0.4 (± 13.22)	
DAY 330 (n=90, 48, 0)	5.2 (± 14.49)	999 (± 999)	-1.5 (± 10.58)	
DAY 360 (n=90, 48, 0)	3.0 (± 15.12)	999 (± 999)	-1.5 (± 9.98)	
DAY 510 (n=0, 0, 138)	999 (± 999)	6.3 (± 16.19)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 139)	999 (± 999)	4.9 (± 15.56)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in PCSK9 from baseline up to Day 720

End point title	Percent change in PCSK9 from baseline up to Day 720

End point description:

Percentage change in proprotein convertase subtilisin/kexin type 9 (PCSK9) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	136	48	
Units: Percent change in PCSK9				
arithmetic mean (standard deviation)				
DAY 90 (n=89, 47, 0)	-67.8 (± 15.17)	999 (± 999)	11.6 (± 46.61)	
DAY 150 (n=90, 47, 0)	-72.3 (± 11.37)	999 (± 999)	3.8 (± 36.95)	
DAY 330 (n=89, 47, 0)	-72.9 (± 12.12)	999 (± 999)	4.8 (± 34.50)	
DAY 360 (n=89, 48, 0)	-72.0 (± 10.47)	999 (± 999)	11.7 (± 57.77)	
DAY 510 (n=0, 0, 136)	999 (± 999)	-74.3 (± 10.46)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 136)	999 (± 999)	-71.6 (± 13.42)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolut change in PCSK9 from baseline up to Day 720

End point title	Absolut change in PCSK9 from baseline up to Day 720

End point description:

Absolute change in proprotein convertase subtilisin/kexin type 9 (PCSK9) from baseline to each assessment time up to Day 720.

End point type	Secondary

End point timeframe:

Baseline, up to Day 720

End point values	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	136	48	
Units: ng/mL				
arithmetic mean (standard deviation)				
DAY 90 (n=89, 47, 0)	-259.6 (± 121.5)	999 (± 999)	2.1 (± 223.16)	
DAY 150 (n=90, 47, 0)	-274.8 (± 116.2)	999 (± 999)	-27.7 (± 210.44)	
DAY 330 (n=89, 47, 0)	-278.2 (± 119.8)	999 (± 999)	-23.9 (± 210.85)	
DAY 360 (n=89, 48, 0)	-275.4 (± 117.2)	999 (± 999)	-9.1 (± 245.36)	
DAY 510 (n=0, 0, 136)	999 (± 999)	-288.1 (± 156.9)	999 (± 999)	
Day 720 (study completion) (n=0, 0, 136)	999 (± 999)	-279.5 (± 159.2)	999 (± 999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 90 days post treatment or 30 days after last study visit, whichever was longer, up to a maximum duration of approximately 2 years.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Part 1- Inclisiran

Reporting group description:

Inclisiran sodium 300 mg subcutaneous (sc) injection (given at Days 1, 90 and 270)

Reporting group title	Part 2 – Inclisiran (Total)

Reporting group description:

Inclisiran sodium 300 mg sc injection (given at Days 450 and 630). In addition, participants assigned to placebo in Part 1 received inclisiran sodium 300 mg sc injection on Day 360, while participants assigned to inclisiran in Part 1 received placebo sc injection on Day 360

Reporting group title	Part 1 - Placebo

Reporting group description:

Placebo sc injection (given at Day 1, 90 and 270)

Serious adverse events	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 93 (3.23%)	6 / 139 (4.32%)	1 / 48 (2.08%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 93 (0.00%)	1 / 139 (0.72%)	0 / 48 (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			
Concussion			
subjects affected / exposed	0 / 93 (0.00%)	1 / 139 (0.72%)	0 / 48 (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 disorders			

Varicose vein			
subjects affected / exposed	0 / 93 (0.00%)	1 / 139 (0.72%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Status migrainosus			
subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 93 (0.00%)	1 / 139 (0.72%)	0 / 48 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 93 (1.08%)	1 / 139 (0.72%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 93 (0.00%)	1 / 139 (0.72%)	0 / 48 (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
Infections and infestations			
Dengue fever			
subjects affected / exposed	1 / 93 (1.08%)	0 / 139 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Part 1- Inclisiran	Part 2 – Inclisiran (Total)	Part 1 - Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 93 (61.29%)	52 / 139 (37.41%)	29 / 48 (60.42%)
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	3 / 93 (3.23%)	1 / 139 (0.72%)	1 / 48 (2.08%)
occurrences (all)	3	1	1
Nervous system disorders			
Migraine			
subjects affected / exposed	4 / 93 (4.30%)	2 / 139 (1.44%)	0 / 48 (0.00%)
occurrences (all)	4	2	0
Headache			
subjects affected / exposed	12 / 93 (12.90%)	6 / 139 (4.32%)	3 / 48 (6.25%)
occurrences (all)	14	8	3
Syncope			
subjects affected / exposed	5 / 93 (5.38%)	1 / 139 (0.72%)	0 / 48 (0.00%)
occurrences (all)	5	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 93 (4.30%)	0 / 139 (0.00%)	1 / 48 (2.08%)
occurrences (all)	4	0	2
Influenza like illness			
subjects affected / exposed	4 / 93 (4.30%)	2 / 139 (1.44%)	3 / 48 (6.25%)
occurrences (all)	5	2	5
Injection site pain			
subjects affected / exposed	4 / 93 (4.30%)	4 / 139 (2.88%)	2 / 48 (4.17%)
occurrences (all)	7	7	2
Injection site reaction			
subjects affected / exposed	8 / 93 (8.60%)	5 / 139 (3.60%)	1 / 48 (2.08%)
occurrences (all)	10	5	2
Malaise			
subjects affected / exposed	0 / 93 (0.00%)	0 / 139 (0.00%)	2 / 48 (4.17%)
occurrences (all)	0	0	2
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	5 / 93 (5.38%)	0 / 139 (0.00%)	1 / 48 (2.08%)
occurrences (all)	8	0	1
Nausea			
subjects affected / exposed	4 / 93 (4.30%)	4 / 139 (2.88%)	1 / 48 (2.08%)
occurrences (all)	4	4	2
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 93 (3.23%)	6 / 139 (4.32%)	2 / 48 (4.17%)
occurrences (all)	3	6	2
Infections and infestations			
COVID-19			
subjects affected / exposed	17 / 93 (18.28%)	7 / 139 (5.04%)	12 / 48 (25.00%)
occurrences (all)	17	7	12
Gastroenteritis			
subjects affected / exposed	4 / 93 (4.30%)	3 / 139 (2.16%)	1 / 48 (2.08%)
occurrences (all)	4	4	1
Influenza			
subjects affected / exposed	10 / 93 (10.75%)	11 / 139 (7.91%)	6 / 48 (12.50%)
occurrences (all)	11	11	8
Nasopharyngitis			
subjects affected / exposed	13 / 93 (13.98%)	14 / 139 (10.07%)	9 / 48 (18.75%)
occurrences (all)	14	18	11
Pharyngitis			
subjects affected / exposed	4 / 93 (4.30%)	1 / 139 (0.72%)	2 / 48 (4.17%)
occurrences (all)	4	3	2
Upper respiratory tract infection			
subjects affected / exposed	6 / 93 (6.45%)	4 / 139 (2.88%)	2 / 48 (4.17%)
occurrences (all)	10	5	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2022	The purpose of Amendment 1 was to reduce the sample size of the study from approximately 150 participants to a minimum of 102 participants. The revised sample size was based on a careful review of all existing evidence, including new important data available, i.e., the meanwhile well-established, favorable efficacy and safety profile of inclisiran in adults, the comprehensive, supportive non-clinical studies, new re-assuring study results in pediatric patients for drugs with a similar (i.e., PCSK9-directed) mechanism of action, and positive experience with inclisiran in adolescents from two ongoing studies. The revised sample size of at least 102 participants provides more than 90% power to assess the primary efficacy endpoint, under conservative assumptions of a 30% betweengroup difference and standard deviations of 30/40% for the inclisiran and placebo groups. However, the actual enrollment was 141 participants, which further increased the statistical power for the primary efficacy endpoint and contributed additional safety data.
17 February 2023	The purpose of Amendment 2 was to add an interim analysis (IA) for the PK data collected on Day 1.

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: