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Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Inclisiran (KJX839)

Trial Indication(s)

Elevated (serum) LDL-C

Protocol Number

CKJX839A12105

Protocol Title

A placebo-controlled, participant, investigator and sponsor blinded, randomized study to evaluate the pharmacokinetics and pharmacodynamics of inclisiran treatment given as single subcutaneous injection in Chinese participants with elevated low-density lipoprotein cholesterol (LDL-C) despite treatment with LDL-C lowering therapies (ORION-14)

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase 1

Study Start/End Dates

Study Start Date: February 2021 (Actual)
Primary Completion Date: October 2021 (Actual)
Study Completion Date: October 2021 (Actual)

Study Design/Methodology

This was a placebo-controlled, participant, investigator and sponsor-blinded, randomized study to evaluate the pharmacokinetics (PK) and pharmacodynamics (PD) (PCSK9 and LDL-C) of inclisiran sodium given as a single subcutaneous injection in 40 Chinese participants with elevated serum LDL-C on lipid lowering treatment.

Centers

China(3)

Objectives:

Primary objectives:

• Evaluate the pharmacokinetics of inclisiran following a single sub-cutaneous administration in Chinese participants
• Evaluate the effect of inclisiran treatment on plasma proprotein convertase subtilisin/kexin 9 (PCSK9) and serum low-density lipoprotein cholesterol (LDL-C) levels over time

Secondary objectives:

• Evaluate the pharmacodynamic (PD) differences between inclisiran and placebo on plasma PCSK9 and serum LDL-C at Days 30, 60, and 90

• Immunogenicity of inclisiran

• Safety and tolerability

Test Product (s), Dose(s), and Mode(s) of Administration

- Inclisiran Sodium 300 mg x 1 dose at Day 1
- Inclisiran Sodium 100 mg x 1 dose at Day 1
- Placebo x 1 dose at Day 1

Inclisiran sodium and placebo (sterile normal saline) were administered to the participants via sub-cutaneous injections using single-use vials.

Statistical Methods

Pharmacokinetics (PK):

Statistical analysis was performed on inclisiran plasma concentration data and PK parameters.

Inclisiran plasma concentration data were listed by participant, treatment group, and scheduled collection time. Descriptive summary statistics including mean (arithmetic and geometric), standard deviation (SD), coefficient of variation (CV) (arithmetic and geometric), median, minimum, and maximum were provided by dose/visit/sampling time point. The geometric mean and arithmetic mean (SD) plots were also graphically presented for concentration-time data. Missing data or concentrations below the lower limit of quantification (LLOQ) were labeled as such in concentration listings. Concentrations below the LLOQ were treated as zero for summary statistics but not included in the calculation of PK parameters (with the exception of pre-dose concentrations).

Where possible, PK parameters of inclisiran were calculated from the individual concentration-time profiles obtained following the study treatment. Only median values and ranges were given for Tmax (the time to reach maximum peak serum drug concentration after single dose administration(time). Missing data were not imputed.

Pharmacodynamics:
PCSK9 plasma concentration and LDL-C serum concentration were expressed as ng/mL and mg/dL, respectively. Missing data or concentrations below LLOQ were labeled as such in concentration listings. Both PCSK9 plasma concentrations and LDL-C serum concentrations were summarized by treatment (placebo, inclisiran sodium 100 mg and 300 mg) and time point.

Safety:
The safety and tolerability variables were the number, percentage, severity and study drug relationship of Adverse Events (AEs) and Serious Adverse Events (SAEs), reporting of deaths, clinical laboratory evaluations (hematology, coagulation, biochemistry, and

urinalysis), electrocardiograms (ECGs), vital signs (body temperature, blood pressure and pulse rate), and pregnancy reporting, as well as testing for binding and neutralizing anti-inclisiran antibodies.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
1. Written informed consent must be obtained before any assessment is performed.
2. Male or female participants ≥ 18 years of age at screening
3. Participants should meet fasting serum LDL-C ≥ 100 mg/dL (≥ 2.6 mmol/L) at screening
4. Participants should meet fasting triglyceride < 400 mg/dL (< 4.52 mmol/L) at screening
5. Participants should be receiving a maximally tolerated dose of statin#.
6. For all participants, all the lipid-lowering therapy/ies (such as but not limited to statins and/or ezetimibe) should have remained stable (stable dose and no medication change) for ≥ 30 days before screening with no planned medication or dose change during study participation. #Maximum tolerated dose was defined as the maximum dose of statin that could be taken on a regular basis without intolerable AEs.
7. Participants not receiving statin must have a documented evidence of intolerance to all doses of at least 2 different statins (or the corresponding local definition of complete intolerance to statins)

Exclusion Criteria:
1. Participants diagnosed with any of following: homozygous familial hypercholesterolemia, New York Heart Association class III & IV heart failure, poorly controlled Type 2 diabetes, uncontrolled severe hypertension, active liver disease, HIV infection or any uncontrolled or serious disease;
2. History of drug abuse or unhealthy alcohol use, malignancy of any organ system, or allergy to the investigational compound/compound class;
3. Major adverse cardiovascular event within 3 months prior to randomization;
4. Calculated glomerular filtration rate ≤30 mL/min by estimated glomerular filtration rate (eGFR) using standardized clinical methodology;
5. Use of other investigational drugs or planned use of other investigational products or devices;
6. Women of child-bearing potential unless they are using basic methods of contraception during dosing of investigational drug (total abstinence, sterilization, barrier methods, hormonal contraception, intrauterine device);
7. Treatment with monoclonal antibodies inhibiting PCSK9 within 90 days prior to screening.

Other protocol-defined inclusion/exclusion criteria may apply

Participant Flow Table

Overall Study

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	300 mg inclisiran sodium (equivalent to 284 mg inclisiran)	Placebo	Total
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1	Placebo x 1 dose at Day 1	
Started	15	15	10	40
Completed	15	15	10	40
Not Completed	0	0	0	0

Baseline Characteristics

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	300 mg inclisiran sodium (equivalent to 284 mg inclisiran)	Placebo	Total
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg	300 mg inclisiran sodium (equivalent to 284 mg	Placebo x 1 dose at Day 1	

	inclisiran) x 1 dose at Day 1	inclisiran) x 1 dose at Day 1		
Number of Participants [units: participants]	15	15	10	40
Age Continuous[1] (units: Years) Mean ± Standard Deviation				
	62.6±10.53	59.5±7.45	57.3±9.59	60.1±9.25
Sex: Female, Male (units: Participants) Count of Participants (Not Applicable)				
Female	11	12	6	29
Male	4	3	4	11
Race/Ethnicity, Customized (units: Participants)				
Asian	15	15	10	40

[1] Age of Participants

Primary Outcome Result(s)

Pharmacokinetics parameters of inclisiran: Cmax

(Time Frame: 0-48 hours post-dose)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**
Arm/Group Description	100 mg inclisiran sodium	300 mg inclisiran sodium

	(equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	(equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	15	15
Pharmacokinetics parameters of inclisiran: Cmax (units: ng/mL) Mean ± Standard Deviation		
	227 ± 91.6	775 ± 339

Pharmacokinetics parameters of inclisiran: Tmax

(Time Frame: 0-48 hours post-dose)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	15	15
Pharmacokinetics parameters of inclisiran: Tmax		

(units: Hour (h)) Median (Full Range)		
	8.00 (0.500 to 12.0)	6.00 (1.00 to 12.0)

Pharmacokinetics parameters of inclisiran: T1/2

(Time Frame: 0-48 hours post-dose)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	1	12
Pharmacokinetics parameters of inclisiran: T1/2 (units: Hour (h)) Median (Full Range)		
	6.65 (6.65 to 6.65)	6.42 (2.98 to 8.56)

Pharmacokinetics parameters of inclisiran: AUC:0-24 hours

(Time Frame: 0-24 hours post-dose)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	300 mg inclisiran sodium (equivalent to 284 mg inclisiran)
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	15	15
Pharmacokinetics parameters of inclisiran: AUC:0-24 hours (units: h*ng/mL) Median (Full Range)		
AUC0-24h	3090 (1920 to 4150)	10700 (6600 to 23500)

Pharmacokinetics parameters of inclisiran: AUC:0-48 hours

(Time Frame: 0-48 hours post-dose)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	300 mg inclisiran sodium (equivalent to 284 mg inclisiran)
Arm/Group Description	100 mg inclisiran sodium	300 mg inclisiran sodium

	(equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	(equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	13	13
Pharmacokinetics parameters of inclisiran: AUC:0-48 hours (units: h*ng/mL) Median (Full Range)		
AUC0-48h	3270 (2390 to 4060)	10900 (7620 to 24800)

Pharmacokinetics parameters of inclisiran: AUClast

(Time Frame: 0-48 hours post-dose)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	15	15
Pharmacokinetics parameters of inclisiran:		

AUClast (units: h*ng/mL) Median (Full Range)		
AUClast	2760 (1580 to 4140)	10700 (7410 to 24700)

Percentage change in Proprotein convertase subtilisin kexin 9 (PCSK9) from baseline overtime

(Time Frame: Baseline to Days 5, 8, 15, 30, 60 and 90)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	14	15
Percentage change in Proprotein convertase subtilisin kexin 9 (PCSK9) from baseline overtime (units: Percentage) Mean ± Standard Deviation		
Day 5	-33.7 ± 17.6	-46.2 ± 9.2
Day 8	-47.3 ± 17.3	-64.8 ± 9.4
Day 15	-58.9 ± 17.4	-76.1 ± 9.7
Day 30	-67.8 ± 9.5	-80.3 ± 6.2
Day 60	-64.4 ± 13.5	-76.4 ± 7.0

Day 90	-56.4 ± 20.3	-74.9 ± 7.5

Percentage change in Low density lipoprotein cholesterol (LDL-C) from baseline overtime

(Time Frame: Baseline to Days 5, 8, 15, 30, 60 and 90)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	14	15
Percentage change in Low density lipoprotein cholesterol (LDL-C) from baseline overtime (units: Percentage) Mean ± Standard Deviation		
Day 5	-11.7 ± 16.1	-19.7 ± 16.6
Day 8	-19.7 ± 19.8	-29.5 ± 20.9
Day 15	-43.8 ± 14.5	-54.4 ± 12.8
Day 30	-52.9 ± 14.2	-63.9 ± 13.2
Day 60	-53.9 ± 13.5	-59.1 ± 21.4
Day 90	-49.6 ± 15.5	-58.3 ± 21.9

Secondary Outcome Result(s)

Percent change from baseline to Days 30, 60 and 90 in PD parameter Proprotein convertase subtilisin kexin 9 (PCSK9)

(Time Frame: Days 30, 60 and 90)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	300 mg inclisiran sodium (equivalent to 284 mg inclisiran)	Placebo
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1	Placebo x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	14	15	10
Percent change from baseline to Days 30, 60 and 90 in PD parameter Proprotein convertase subtilisin kexin 9 (PCSK9) (units: Percentage) Least Squares Mean (95% Confidence Interval)			
Day 30	-68.6 (-76.1 to -61.2)	-78.7 (-86.2 to -71.2)	-1.3 (-10.0 to 7.5)
Day 60	-65.2 (-73.3 to -57.2)	-75.2 (-83.1 to -67.3)	6.4 (-3.0 to 15.8)
Day 90	-57.2 (-66.9 to -47.4)	-73.7 (-83.3 to -64.2)	3.0 (-8.4 to 14.5)

Statistical Analysis

Groups	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran), Placebo	Day 30
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-67.4	
95 % Confidence Interval 2-Sided	-78.7 to -56.0	

Statistical Analysis

Groups	300 mg inclisiran sodium (equivalent to 284 mg inclisiran), Placebo	Day 30
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-77.4	
95 % Confidence Interval 2-Sided	-89.1 to -65.8	

Statistical Analysis

Groups	100 mg inclisiran sodium (equivalent to 94.5 mg	Day 60

	inclisiran), Placebo
P Value	<0.0001
Method	Other Mixed Model Repeated Measures
Mean Difference (Final Values)	-71.6
95 % Confidence Interval 2-Sided	-83.9 to -59.4

Statistical Analysis

Groups	300 mg inclisiran sodium (equivalent to 284 mg inclisiran), Placebo	Day 60
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-81.6	
95 % Confidence Interval 2-Sided	-94.1 to -69.1	

Statistical Analysis

Groups	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran), Placebo	Day 90

P Value	<0.0001
Method	Other Mixed Model Repeated Measures
Mean Difference (Final Values)	-60.2
95 % Confidence Interval 2-Sided	-75.1 to -45.2

Statistical Analysis

Groups	300 mg inclisiran sodium (equivalent to 284 mg inclisiran), Placebo	Day 90
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-76.7	
95 % Confidence Interval 2-Sided	-91.8 to -61.7	

Percent change from baseline to Days 30, 60 and 90 in PD parameter Low density lipoprotein cholesterol (LDL-C)

(Time Frame: Baseline to Days 30, 60 and 90)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**	**Placebo**

Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1	Placebo x 1 dose at Day 1
Number of Participants Analyzed [units: participants]	14	15	10
Percent change from baseline to Days 30, 60 and 90 in PD parameter Low density lipoprotein cholesterol (LDL-C) (units: Percentage) Least Squares Mean (95% Confidence Interval)			
Day 30	-53.0 (-61.3 to -44.6)	-63.3 (-71.6 to -55.1)	-17.0 (-26.9 to -7.1)
Day 60	-54.0 (-63.5 to -44.5)	-58.8 (-68.1 to -49.6)	-16.7 (-28.0 to -5.4)
Day 90	-49.7 (-60.2 to -39.2)	-58.1 (-68.2 to -47.9)	-19.5 (-31.9 to -7.1)

Statistical Analysis

Groups	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran), Placebo	Day 30
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	

Mean Difference (Final Values)	-36.0
95 % Confidence Interval 2-Sided	-48.9 to -23.1

Statistical Analysis

Groups	300 mg inclisiran sodium (equivalent to 284 mg inclisiran), Placebo	Day 30
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-46.4	
95 % Confidence Interval 2-Sided	-59.3 to -33.4	

Statistical Analysis

Groups	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran), Placebo	Day 60
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	

Mean Difference (Final Values)	-37.3
95 % Confidence Interval 2-Sided	-52.1 to -22.6

Statistical Analysis

Groups	300 mg inclisiran sodium (equivalent to 284 mg inclisiran)	Day 60
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-42.1	
95 % Confidence Interval 2-Sided	-56.8 to -27.4	

Statistical Analysis

Groups	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	Day 90
P Value	0.0006	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-30.2	

95 % Confidence Interval 2-Sided	-46.4 to -14.0

Statistical Analysis

Groups	300 mg inclisiran sodium (equivalent to 284 mg inclisiran), Placebo	Day 90
P Value	<0.0001	
Method	Other Mixed Model Repeated Measures	
Mean Difference (Final Values)	-38.6	
95 % Confidence Interval	-54.7 to -22.5	

Rate of formation of anti-drug antibodies to Inclisiran

(Time Frame: Baseline, Days 30 and 90)

	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran)	**300 mg inclisiran sodium (equivalent to 284 mg inclisiran)**	**Placebo**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1	Placebo x 1 dose at Day 1

Number of Participants Analyzed [units: participants]	15	15	10
Rate of formation of anti-drug antibodies to Inclisiran (units: Participants)			
Baseline	0	0	0
Day 30	0	0	0
Day 90	0	0	0

Safety Results

All-Cause Mortality

	Inclisiran sodium 100 mg (equivalent to 94.5 mg inclisiran) N = 15	**Inclisiran sodium 300 mg (equivalent to 284 mg inclisiran) N = 15**	**Placebo N = 10**	**Total N = 40**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1	Placebo x 1 dose at Day 1	Total
Total participants affected	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Adverse Events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum duration of approximately 9 months.
Additional Description	Any sign or symptom that occurs during the study treatment plus the 30 days post treatment.
Source Vocabulary for Table Default	MedDRA (24.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	1%

	Inclisiran sodium 100 mg (equivalent to 94.5 mg inclisiran) N = 15	**Inclisiran sodium 300 mg (equivalent to 284 mg inclisiran) N = 15**	**Placebo N = 10**	**Total N = 40**
Arm/Group Description	100 mg inclisiran sodium (equivalent to 94.5 mg inclisiran) x 1 dose at Day 1	300 mg inclisiran sodium (equivalent to 284 mg inclisiran) x 1 dose at Day 1	Placebo x 1 dose at Day 1	Total
Total participants affected	7 (46.67%)	12 (80.00%)	5 (50.00%)	24 (60.00%)
Blood and lymphatic system disorders				
Anaemia	0 (0.00%)	2 (13.33%)	0 (0.00%)	2 (5.00%)
Cardiac disorders				
Sinus bradycardia	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.50%)

Eye disorders				
Presbyopia	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Gastrointestinal disorders				
Nausea	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
General disorders and administration site conditions				
Asthenia	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Chest discomfort	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Chest pain	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Injection site bruising	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.50%)
Swelling	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Hepatobiliary disorders				
Hepatic function abnormal	0 (0.00%)	2 (13.33%)	0 (0.00%)	2 (5.00%)
Infections and infestations				
Herpes zoster	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (2.50%)
Investigations				
Activated partial thromboplastin time prolonged	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (2.50%)
Blood creatine phosphokinase increased	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (2.50%)

Blood uric acid increased	2 (13.33%)	0 (0.00%)	1 (10.00%)	3 (7.50%)
Gamma-glutamyltransferase increased	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.50%)
Hepatic enzyme increased	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Neutrophil count decreased	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.50%)
Protein urine present	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Red blood cells urine positive	1 (6.67%)	0 (0.00%)	0 (0.00%)	1 (2.50%)
Transaminases increased	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
White blood cell count decreased	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
White blood cells urine positive	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Metabolism and nutrition disorders				
Decreased appetite	0 (0.00%)	1 (6.67%)	0 (0.00%)	1 (2.50%)
Nervous system disorders				
Dizziness	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (2.50%)
Headache	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (2.50%)
Skin and subcutaneous tissue disorders				
Papule	0 (0.00%)	0 (0.00%)	1 (10.00%)	1 (2.50%)

Conclusion:

Pharmacokinetics:

- Following a single sub-cutaneous injection of inclisiran sodium 100 mg or 300 mg, inclisiran was readily absorbed with a short T1/2. Its inter-participant variability (CV%) was generally moderate.

Pharmacodynamics:

- Inclisiran exhibited rapid, robust, durable, and consistent reductions in PCSK9 and LDL-C after sub-cutaneous administration, in a dose-dependent manner.
- In this study, maximal PCSK9 inhibition and LDL-C reduction were observed after dosing of 300 mg inclisiran sodium.

Safety:

- Inclisiran is generally safe and well tolerated in Chinese participants, and no new safety concerns were identified with either of the inclisiran sodium doses administered in this study.
- There were no deaths or serious adverse events (SAEs) reported in this study and no participants discontinued study due to an adverse event (AE).

Date of Clinical Trial Report

27-September-2022