Clinical trial results:
A Multi-center, Open-label Study to Evaluate the Safety, Pharmacokinetics, and Efficacy of Lanadelumab (SHP643) in Chinese Subjects with Hereditary Angioedema

Summary

EudraCT number	2023-001105-31
Trial protocol	Outside EU/EEA
Global end of trial date	28 November 2023

Results information

Result version number	v1 (current)
This version publication date	09 June 2024
First version publication date	09 June 2024

Trial information

Trial identification

Sponsor protocol code	SHP643-304

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05460325
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Takeda
Sponsor organisation address	95 Hayden Avenue, Lexington, United States, MA 02421
Public contact	Study Director, Takeda, trialdisclosures@takeda.com
Scientific contact	Study Director, Takeda, trialdisclosures@takeda.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 November 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety of repeated subcutaneous (SC) administrations of lanadelumab in Chinese participants with hereditary angioedema (HAE).

Protection of trial subjects:

Each participant signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 June 2022
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	China: 20
Worldwide total number of subjects	20
EEA total number of subjects	0

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)	1
Adults (18-64 years)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 4 investigative sites in China from 22 June 2022 to 28 November 2023.

Pre-assignment

Screening details:

Total 20 participants with diagnosis of hereditary angioedema(HAE) were enrolled in Run-in Period of 4-8 weeks.Participants who experienced ≥1.0 investigator-confirmed HAE attack per 4 weeks during Run-in Period & who remained eligible per inclusion & exclusion criteria entered the 26-week lanadelumab Treatment Period to receive lanadelumab 300 mg.

Period 1

Period 1 title	Run-in Period (4 or up to 8 Weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lanadelumab 300 mg

Arm description:

Participants received lanadelumab 300 mg, subcutaneously (SC), once every two weeks (Q2W) for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Lanadelumab
Investigational medicinal product code	
Other name	SHP643, TAKHZYRO, TAK-743, DX-2930, Lanadelumab Injection, Lanadelumab-flyo
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Lanadelumab 300 mg was administered SC, Q2W for 26 weeks.

Number of subjects in period 1	Lanadelumab 300 mg
Started	20
Completed	20

Period 2

Period 2 title	Treatment Period (Weeks 1 to 26)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lanadelumab 300 mg

Arm description:

Participants received lanadelumab 300 mg, subcutaneously (SC), once every two weeks (Q2W) for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Lanadelumab
Investigational medicinal product code	
Other name	SHP643, TAKHZYRO, TAK-743, DX-2930, Lanadelumab Injection, Lanadelumab-flyo
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received lanadelumab 300 mg, SC, Q2W.

Number of subjects in period 2	Lanadelumab 300 mg
Started	20
Completed	20

Period 3

Period 3 title	Safety Follow-up Period (Weeks 27 to 30)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lanadelumab 300 mg

Arm description:

Participants received lanadelumab 300 mg, subcutaneously (SC), once every two weeks (Q2W) for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Lanadelumab
Investigational medicinal product code	
Other name	SHP643, TAKHZYRO, TAK-743, DX-2930, Lanadelumab Injection, Lanadelumab-flyo
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
Lanadelumab 300 mg was administered SC, Q2W for 26 weeks.

Number of subjects in period 3	Lanadelumab 300 mg
Started	20
Completed	20

Baseline characteristics

Reporting groups	
Reporting group title	Lanadelumab 300 mg
Reporting group description:	
Participants received lanadelumab 300 mg, subcutaneously (SC), once every two weeks (Q2W) for 26 weeks.	

Reporting group values	Lanadelumab 300 mg	Total	
Number of subjects	20	20	
Age Categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	37.8		
standard deviation	± 11.60	-	
Gender categorical			
Units: Subjects			
Female	13	13	
Male	7	7	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	20	20	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	0	0	
More than one race	0	0	
Unknown or Not Reported	0	0	
Region of Enrollment			
Units: Subjects			
China China	20	20	
Weight			
Units: kilograms (kg)			
arithmetic mean	67.65		
standard deviation	± 13.551	-	
Body Mass Index (BMI)			
BMI = weight (kg)/[height (m)^2]			
Units: kilograms per meter square (kg/m^2)			
arithmetic mean	24.18		
standard deviation	± 3.927	-	
Height			
Units: centimeter (cm)			
arithmetic mean	166.83		
standard deviation	± 7.973	-	

End points

End points reporting groups

Reporting group title	Lanadelumab 300 mg
Reporting group description:	
Participants received lanadelumab 300 mg, subcutaneously (SC), once every two weeks (Q2W) for 26 weeks.	
Reporting group title	Lanadelumab 300 mg
Reporting group description:	
Participants received lanadelumab 300 mg, subcutaneously (SC), once every two weeks (Q2W) for 26 weeks.	
Reporting group title	Lanadelumab 300 mg
Reporting group description:	
Participants received lanadelumab 300 mg, subcutaneously (SC), once every two weeks (Q2W) for 26 weeks.	

Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Adverse Events of Special Interest (AESIs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs) and Adverse Events of Special Interest (AESIs)[1]

End point description:

TEAE=an adverse event (AE) with onset at the time of or following initial dosing with study drug (lanadelumab), or medical conditions present prior to the start of study drug but increasing in severity or relationship at the time of or following the start of treatment, up to the last follow-up visit. An SAE is any untoward clinical manifestation of signs, symptoms or outcomes whether considered related to investigational product or not and at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of hospitalization, results in persistent or significant disability/incapacity, congenital abnormality/birth defect, an important medical event. Hypersensitivity reactions and events of disordered coagulation were considered as AESIs. Adverse events were classified as HAE attack and non-HAE attack reported AEs and are categorized accordingly in this outcome measure. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Primary

End point timeframe:

From first dose of study drug up to end of study (up to Day 210)

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: Only descriptive analysis was planned for this endpoint.

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants				
TEAEs: Non-Angioedema Attack	17			
TEAEs: Angioedema Attack	4			
SAEs: Non-Angioedema Attack	1			
SAEs: Angioedema Attack	0			
AESIs: Non-Angioedema Attack	0			
AESIs: Angioedema Attack	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Changes in Clinical Laboratory Parameters

End point title	Number of Participants With Clinically Meaningful Changes in Clinical Laboratory Parameters[2]

End point description:

Laboratory parameters included clinical chemistry, hematology, coagulation, urinalysis, and serology. Clinically meaningful laboratory parameters assessment was based on investigator interpretation. Number of participants with clinically meaningful changes in laboratory parameters (including clinical chemistry, hematology, coagulation, urinalysis, and serology) were reported. The Full Analysis Set (FAS) included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Primary

End point timeframe:

From first dose of study drug up to end of study (up to Day 210)

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: Only descriptive analysis was planned for this endpoint.

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Changes in Vital Sign Abnormalities

End point title	Number of Participants With Clinically Meaningful Changes in Vital Sign Abnormalities[3]

End point description:

Vital signs included measurement of blood pressure, heart rate, body temperature, and respiratory rate. Clinically meaningful vital signs assessment was based on investigator interpretation. Number of participants with clinically meaningful changes in vital signs were reported. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Primary

End point timeframe:

From first dose of study drug up to end of study (up to Day 210)

Notes:

[3] - 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: Only descriptive analysis was planned for this endpoint.

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Meaningful Changes in Electrocardiogram (ECG)

End point title	Number of Participants With Clinically Meaningful Changes in Electrocardiogram (ECG)[4]

End point description:

ECG included heart rate, PR interval, QRS duration, QT interval, corrected QT interval (QTc) interval, QT corrected for heart rate by Fridericia's cube root formula (QTcF) interval, and QT corrected for heart rate by Bazett formula (QTcB) interval. Clinically meaningful ECG assessment was based on investigator interpretation. Number of participants with clinically meaningful changes in ECG were reported. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Primary

End point timeframe:

From first dose of study drug up to end of study (up to Day 210)

Notes:

[4] - 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: Only descriptive analysis was planned for this endpoint.

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Clinically Significant Physical Examination Abnormalities on Day 182

End point title	Number of Participants With Clinically Significant Physical Examination Abnormalities on Day 182[5]

End point description:

Physical examination findings by body system were classified as height and weight, general appearance, ears, nose and throat, head and neck, ophthalmological, respiratory, cardiovascular, abdomen, neurological, extremities, dermatological, and lymphatic. Number of participants with clinically

significant changes in physical examination findings per investigator interpretation were reported. Only categories with at least one participant with event are reported. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Primary

End point timeframe:

Day 182

Notes:

[5] - 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: Only descriptive analysis was planned for this endpoint.

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants				
Dermatologic System	2			
Extremities	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Lanadelumab

End point title	Plasma Concentrations of Lanadelumab

End point description:

The Pharmacokinetic (PK) Set included all participants in the FAS who had at least 1 evaluable post-dose PK concentration value. 'n' signifies the number of participants with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Anytime on Days 0 and 210; and pre-dose on Days 14, 56, 98, 140, 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 0 (n=20)	7.64 (± 24.096)			
Day 14: Pre-dose (n=17)	12336.47 (± 4531.386)			
Day 56: Pre-dose (n=19)	24857.89 (± 6950.725)			
Day 98: Pre-dose (n=20)	24170.00 (± 7260.426)			
Day 140: Pre-dose (n=19)	23821.05 (± 8808.870)			

Day 182: Pre-dose (n=20) Day 210 (n=20)	24610.00 (± 6599.673) 12048.00 (± 3268.807)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Kallikrein (pKal) Activity

End point title	Plasma Kallikrein (pKal) Activity

End point description:

pKal activity was measured by cleaved high molecular weight kininogen (cHMWK) level (i.e., plasma concentrations of cHMWK). The Pharmacodynamic (PD) Set included all participants in the FAS who had at least 1 evaluable post-dose PD concentration value. 'n' signifies the number of participants with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Anytime on Days 0 and 210; and pre-dose on Days 14, 56, 98, 140, 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 0 (n=20) Day 14: Pre-dose (n=17) Day 56: Pre-dose (n=19) Day 98: Pre-dose (n=20) Day 140: Pre-dose (n=19) Day 182: Pre-dose (n=20) Day 210 (n=20)	10256.419 (± 3311.3810) 4904.964 (± 1350.4121) 3604.136 (± 1279.8551) 3312.706 (± 1526.8282) 2871.364 (± 1324.5022) 3383.672 (± 1337.0341) 3800.187 (± 1499.9735)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Investigator-Confirmed HAE Attacks During the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Investigator-Confirmed HAE Attacks During the

	Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

An HAE attack was confirmed by following symptoms or signs consistent with an attack in at least one of the following locations: 1) Peripheral angioedema: cutaneous swelling involving an extremity, the face, neck, torso, and/or genitourinary region; 2) Abdominal angioedema: abdominal pain, with or without abdominal distention, nausea, vomiting, or diarrhea; 3) Laryngeal angioedema: stridor, dyspnea, difficulty speaking, difficulty swallowing, throat tightening, or swelling of the tongue, palate, uvula, or larynx. Treatment period attack rate per month is calculated as the number of investigator-confirmed HAE attacks occurring during that treatment period divided by number of days the participant contributed to that treatment period multiplied by 28 days. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: attacks/month				
arithmetic mean (standard deviation)	0.04 (± 0.139)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Investigator-Confirmed HAE Attacks that Required Acute Treatment During the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Investigator-Confirmed HAE Attacks that Required Acute Treatment During the Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

HAE attack was confirmed by following symptoms consistent with attack in atleast 1 of following locations:1)Peripheral angioedema:cutaneous swelling in extremity,face,neck,torso,and/or genitourinary region;2)Abdominal angioedema:abdominal pain,with/without abdominal distention,nausea,vomiting/diarrhea;3)Laryngeal angioedema:stridor,dyspnea,difficulty speaking,difficulty swallowing,throat tightening/swelling of tongue,palate,uvula/larynx.Acute HAE attacks were managed per investigator’s usual care, including use of individualized acute therapy/rescue medications.Acute therapy/rescue medications included Firazyr,fresh frozen plasma(FFP)/other local standard of care.Treatment period attack rate per month=number of investigator-confirmed HAE attacks requiring acute treatment occurring during that treatment period divided by number of days participant contributed to that treatment period multiplied by 28 days.FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: attacks/month				
arithmetic mean (standard deviation)	0.01 (± 0.034)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Moderate or Severe Investigator-Confirmed HAE Attacks During the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Moderate or Severe Investigator-Confirmed HAE Attacks During the Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

The severity of the investigator-confirmed HAE attacks was defined per the HAE attack assessment and reporting procedures (HAARP) definitions: severe (marked limitation in activity, assistance required), moderate (mild to moderate limitation in activity, some assistance needed). Treatment period attack rate per month is calculated as the number of moderate or severe investigator-confirmed HAE attacks occurring during that treatment period divided by number of days the participant contributed to that treatment period multiplied by 28 days. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: attacks/month				
arithmetic mean (standard deviation)	0.01 (± 0.034)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Maximum Attack Severity During the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Participants with Maximum Attack Severity During the Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

Number of participants with maximum HAE attack severity during the efficacy evaluation period was assessed. HAE attack severity was calculated per participant based on the severity categories as follows: No attack, Mild, Moderate, and Severe. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants				
No Attack	18			
Mild	1			
Moderate	1			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Investigator-confirmed HAE Attack During the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Time to First Investigator-confirmed HAE Attack During the Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

Time to the first investigator-confirmed HAE attack (days) was calculated from the date and time of the first dose of study drug for that efficacy evaluation period to the date and time of the first investigator-confirmed HAE attack after the first dose for the efficacy evaluation period. The time to the first HAE attack was summarized using Kaplan-Meier (KM) estimates. '99999' indicates that median and full range were not evaluable due to low number of participants with events. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: days				
median (full range (min-max))	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved at Least 50%, 70%, 90%, and 100% Reduction in the Investigator-Confirmed Normalized Number of Attacks (NNA) per 4 Weeks Relative to the Run-in Period NNA

End point title	Number of Participants who Achieved at Least 50%, 70%, 90%, and 100% Reduction in the Investigator-Confirmed Normalized Number of Attacks (NNA) per 4 Weeks Relative to the Run-in Period NNA

End point description:

A run-in period of 4 weeks was included to determine the participant's baseline attack rate. This period may be extended up to 8 weeks. The normalized number of investigator-confirmed HAE attacks during efficacy evaluation period was expressed as a monthly (28 days) HAE attack rate relative to the run-in period NNA. Number of participants who achieved at least 50 percent (%), 70%, 90% and 100% reduction in the investigator-confirmed NNA per 4 weeks relative to the run-in period normalized NNA for the efficacy evaluation periods was assessed. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants				
≥50% Reduction	20			
≥70% Reduction	20			
≥90% Reduction	19			
100% Reduction	18			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved NNA <1.0 per 4 Weeks for the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Participants who Achieved NNA <1.0 per 4 Weeks for the Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

The normalized number of investigator-confirmed HAE attacks during the efficacy evaluation period was expressed as a monthly (28 days) HAE attack rate. Attack rate was calculated for each participant as the number of attacks occurring during the specified period divided by the number of days the participant contributed to the specified period multiplied by 28 days. Number of participants who achieved NNA <1.0 per 4 weeks for the efficacy evaluation period were assessed. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved Investigator-confirmed HAE Attack-Free Status During the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Participants who Achieved Investigator-confirmed HAE Attack-Free Status During the Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

An HAE attack was confirmed by following symptoms or signs consistent with an attack in at least one of the following locations: 1) Peripheral angioedema: cutaneous swelling involving an extremity, the face, neck, torso, and/or genitourinary region; 2) Abdominal angioedema: abdominal pain, with or without abdominal distention, nausea, vomiting, or diarrhea; 3) Laryngeal angioedema: stridor, dyspnea, difficulty speaking, difficulty swallowing, throat tightening, or swelling of the tongue, palate, uvula, or larynx. A participant was considered as attack free if the participant had no investigator-confirmed HAE attacks during the efficacy evaluation period. Number of participants who achieved attack-free status for the efficacy evaluation periods were assessed. The FAS included all participants who received at least 1 dose of lanadelumab (IP).

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants	18			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Neutralizing or Non-neutralizing Antidrug Antibodies (ADA) in Plasma

End point title	Number of Participants With Neutralizing or Non-neutralizing Antidrug Antibodies (ADA) in Plasma

End point description:

Number of participants with neutralizing or non-neutralizing ADA in plasma were assessed. The FAS included all participants who received at least 1 dose of lanadelumab (IP). 'n' signifies the number of participants with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Anytime on Days 0 and 210; and pre-dose on Days 14, 56, 98, 140, 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: participants				
Day 0 (n=20)	1			
Day 56: Pre-dose (n=19)	0			
Day 98: Pre-dose (n=20)	0			
Day 140: Pre-dose (n=19)	1			
Day 182: Pre-dose (n=20)	1			
Day 210 (n=20)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Lanadelumab by Immunogenicity Result

End point title	Plasma Concentrations of Lanadelumab by Immunogenicity Result

End point description:

The effect of presence or absence of neutralizing or non-neutralizing ADA in plasma on the lanadelumab plasma concentrations was assessed. '9999' indicates that data was not available as no participants were analyzed at the specified time point. '99999' indicates that standard deviation (SD) was not estimable for a single participant. The PK set included all participants in the FAS who had at least 1 evaluable post-dose PK concentration value. 'n' signifies the number of participants with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Anytime on Days 0 and 210; and pre-dose on Days 56, 98, 140, 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 0: Positive ADA Result (n=1)	0.00 (± 99999)			

Day 0: Negative ADA Result (n=19)	8.04 (± 24.687)			
Day 56: Pre-dose: Positive ADA Result (n=0)	9999 (± 9999)			
Day 56: Pre-dose: Negative ADA Result (n=19)	24857.89 (± 6950.725)			
Day 98: Pre-dose: Positive ADA Result (n=0)	9999 (± 9999)			
Day 98: Pre-dose: Negative ADA Result (n=20)	24170.00 (± 7260.426)			
Day 140: Pre-dose: Positive ADA Result (n=1)	16700.00 (± 99999)			
Day 140: Pre-dose: Negative ADA Result (n=18)	24216.67 (± 8888.873)			
Day 182: Pre-dose: Positive ADA Result (n=1)	27800.00 (± 99999)			
Day 182: Pre-dose: Negative ADA Result (n=19)	24442.11 (± 6736.494)			
Day 210: Positive ADA Result (n=3)	13800.00 (± 624.500)			
Day 210: Negative ADA Result (n=17)	11738.82 (± 3458.715)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Kallikrein Activity cHMWK by Immunogenicity Result

End point title	Plasma Kallikrein Activity cHMWK by Immunogenicity Result

End point description:

The effect of presence or absence of neutralizing or non-neutralizing ADA in plasma on the cHMWK levels was assessed. The PD set included all participants in the FAS who had at least 1 evaluable post-dose PD concentration value. '9999' indicates that data was not available as no participants were analysed at the specified time point. '99999' indicates that SD was not estimable for a single participant. 'n' signifies the number of participants with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Anytime on Days 0 and 210; and pre-dose on Days 56, 98, 140, 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 0: Positive ADA Result (n=1)	13346.780 (± 99999)			
Day 0: Negative ADA Result (n=19)	10093.768 (± 3319.0248)			
Day 56: Pre-dose: Positive ADA Result (n=0)	9999 (± 9999)			
Day 56: Pre-dose: Negative ADA Result (n=19)	3604.136 (± 1279.8551)			

Day 98: Pre-dose: Positive ADA Result (n=0)	9999 (± 9999)			
Day 98: Pre-dose: Negative ADA Result (n=20)	3312.706 (± 1526.8282)			
Day 140: Pre-dose: Positive ADA Result (n=1)	3733.890 (± 99999)			
Day 140: Pre-dose: Negative ADA Result (n=18)	2823.446 (± 1345.8483)			
Day 182: Pre-dose: Positive ADA Result (n=1)	4577.960 (± 99999)			
Day 182: Pre-dose: Negative ADA Result (n=19)	3320.814 (± 1342.9683)			
Day 210: Positive ADA Result (n=3)	4938.130 (± 1367.0128)			
Day 210: Negative ADA Result (n=17)	3599.373 (± 1467.1561)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Investigator-confirmed HAE Attacks by Immunogenicity Result and Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Investigator-confirmed HAE Attacks by Immunogenicity Result and Efficacy Evaluation Period of Day 0 Through Day 182

End point description:

Effect of presence or absence of neutralizing or non-neutralizing ADA in plasma on the number of investigator-confirmed HAE attacks during the efficacy evaluation periods was assessed. ''99999' indicates that SD was not estimable for a single participant. The FAS included all participants who received at least 1 dose of lanadelumab (IP). 'n' signifies the number of participants with data available for analyses at the specified timepoint.

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: attacks/month				
arithmetic mean (standard deviation)				
At Least One Positive ADA Result (n=1)	0.00 (± 99999)			
No Positive ADA Result (n=19)	0.04 (± 0.142)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of the study upto follow up (up to Day 210)	
Adverse event reporting additional description:	
The FAS included all participants who received at least 1 dose of lanadelumab (IP).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26

Reporting groups	
Reporting group title	Lanadelumab 300 mg
Reporting group description:	
Participants received lanadelumab 300 mg, SC, Q2W for 26 weeks.	

Serious adverse events	Lanadelumab 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal stenosis			
subjects affected / exposed	1 / 20 (5.00%)		
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	Lanadelumab 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 20 (70.00%)		

Investigations Blood uric acid increased subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 3		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2		
General disorders and administration site conditions Injection site pain subjects affected / exposed occurrences (all) Injection site swelling subjects affected / exposed occurrences (all)	 4 / 20 (20.00%) 16 3 / 20 (15.00%) 7		
Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2 3 / 20 (15.00%) 3 2 / 20 (10.00%) 2		
Hepatobiliary disorders Hepatic function abnormal subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis	 10 / 20 (50.00%) 10		

subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2022	The following changes were made as per Amendment 1: 1) Updated text for the analyses and classification of safety parameters for clarification. 2) Clarified the requirements of repeating test or re-screening. 3) Updated exclusion criteria to indicate that use of long term prophylaxis (LTP) therapy for HAE within 2 weeks prior to entering the run-in period is exclusionary only for adult participants. 4) Added details of "injection report" and "diary card"; removed the "self-administration questionnaire" and "memory aid" to provide clear guidance of the study execution. 5) Added details of the alternatives could be followed during an unanticipated situations like coronavirus disease 2019 (COVID-19) outbreak. 6) Added the subsection of interactive response technology for the investigational product management tasks. 7) Added sentence that alternative approaches such as remote source data review via phone or video could be used for monitoring purpose.
08 February 2023	The following changes were made as per Amendment 2: 1) Added the potential to conduct an interim analysis when approximately 10 participants complete the 26-week treatment period and 4-week follow-up period. 2) Emphasized that for the adolescent participants(<18 years of age) enrolled in the study that reach 18 years of age during study periods, a consent using the most current version of the informed consent form by participant is required. 3) Emphasized that both AESI and SAE should be reported to sponsor or contract research organization (CRO) within 24 hours by investigator by adding AESI reporting requirement in administrative information. 4) Extended the time frame of screening from up to 2 weeks to up to 4 weeks for feasibility of study due to COVID-19. 5) Updated exclusion criteria to specify the requirement to exclude participants using any lanadelumab prior to the study. 6) Removed liver toxicity (EU specific risk) as an important potential risk.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported