Clinical trial results:
A Phase 3 Multi-center, Open-label Study to Evaluate the Efficacy and Safety of Lanadelumab (SHP643) in Japanese Subjects with Hereditary Angioedema

Summary

EudraCT number	2022-002621-98
Trial protocol	Outside EU/EEA
Global end of trial date	26 August 2021

Results information

Result version number	v1 (current)
This version publication date	07 September 2022
First version publication date	07 September 2022

Trial information

Trial identification

Sponsor protocol code	SHP643-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04180163
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shire
Sponsor organisation address	300 Shire Way, Lexington, United States, MA 02421
Public contact	Study Director, Shire, ClinicalTransparency@shire.com
Scientific contact	Study Director, Shire, ClinicalTransparency@shire.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	26 August 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and efficacy of lanadelumab in Japanese participants with HAE Type I or II.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 December 2019
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	Japan: 12
Worldwide total number of subjects	12
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)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 12 participants took part in the study at 10 investigative sites in Japan from 12 December 2019 to 26 August 2021. Participants who rolled over to TAK-743-5007 (NCT04687137) had a 2-week follow-up while others had 4 weeks of follow-up.

Pre-assignment

Screening details:

Subjects were observed in 4-week Baseline Run-in that could be extended upto 8 weeks.Subjects experiencing ≥1.0 angioedema attacks per 4 weeks during Run-in Period,who remained eligible per inclusion criteria entered 52-week lanadelumab Treatment Period(TP)[TP:A + TP:B],followed by upto 4-week Safety Follow-up.Lanadelumab was given only during TPs.

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 q2w or q4w

Arm description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator’s discretion and approval by the Sponsor’s Medical Monitor.

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

Dosage and administration details:

Lanadelumab solution, SC

Number of subjects in period 1	Lanadelumab 300 mg q2w or q4w
Started	12
Completed	12

Period 2

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

Arms

Arm title	Lanadelumab 300 mg q2w or q4w

Arm description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator's discretion and approval by the Sponsor's Medical Monitor.

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

Dosage and administration details:

Lanadelumab solution, SC

Number of subjects in period 2	Lanadelumab 300 mg q2w or q4w
Started	12
Completed	12

Period 3

Period 3 title	Treatment Period B (Weeks 27 to 52)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lanadelumab 300 mg q2w or q4w

Arm description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator's discretion and approval by the Sponsor's Medical Monitor.

Arm type	Experimental

Investigational medicinal product name	Lanadelumab
Investigational medicinal product code	
Other name	DX-2930, TAK-743, SHP643
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Lanadelumab solution, SC

Number of subjects in period 3	Lanadelumab 300 mg q2w or q4w
Started	12
Completed	12

Period 4

Period 4 title	Safety Follow-up Period (Weeks 53 to 56)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Lanadelumab 300 mg q2w or q4w

Arm description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator’s discretion and approval by the Sponsor’s Medical Monitor.

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

Dosage and administration details:

Lanadelumab solution, SC

Number of subjects in period 4	Lanadelumab 300 mg q2w or q4w
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	Lanadelumab 300 mg q2w or q4w

Reporting group description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator's discretion and approval by the Sponsor's Medical Monitor.

Reporting group values	Lanadelumab 300 mg q2w or q4w	Total	
Number of subjects	12	12	
Age Categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 41.9 ± 12.36	 -	
Gender categorical Units: Subjects			
Male	3	3	
Female	9	9	
Race Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	12	12	
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	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	12	12	
Unknown or Not Reported	0	0	
Weight Units: kg arithmetic mean standard deviation	 61.24 ± 10.346	 -	
Height Units: cm arithmetic mean standard deviation	 161.08 ± 9.379	 -	
Body Mass Index (BMI)			
BMI= weight(kg) / height(meter)^2			

Units: kg/m^2			
arithmetic mean	23.80		
standard deviation	± 5.065	-	

End points

End points reporting groups

Reporting group title	Lanadelumab 300 mg q2w or q4w

Reporting group description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator's discretion and approval by the Sponsor's Medical Monitor.

Reporting group title	Lanadelumab 300 mg q2w or q4w

Reporting group description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator's discretion and approval by the Sponsor's Medical Monitor.

Reporting group title	Lanadelumab 300 mg q2w or q4w

Reporting group description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator's discretion and approval by the Sponsor's Medical Monitor.

Reporting group title	Lanadelumab 300 mg q2w or q4w

Reporting group description:

Lanadelumab 300 mg solution, subcutaneously (SC), once every 2 weeks (q2w) for 26 weeks in Treatment Period A. This was followed by Treatment Period B (additional 26 weeks, total of 52 weeks including Treatment Period A) during which participants remained on Treatment Period A regimen or received 300 mg lanadelumab solution once every 4 weeks (q4w) for 26 weeks if well-controlled (attack-free) for 26 consecutive weeks with lanadelumab treatment. The dose frequency change was based on the Investigator's discretion and approval by the Sponsor's Medical Monitor.

Subject analysis set title	Treatment Period A: Non-HAE
Subject analysis set type	Safety analysis

Subject analysis set description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks in Treatment Period A. Non-HAE attack (subset identified in case report form [CRF] as not reported HAE attack) subset participants were included in this arm.

Subject analysis set title	Treatment Period A: HAE
Subject analysis set type	Safety analysis

Subject analysis set description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks in Treatment Period A. HAE attack (subset of AEs identified in CRF as reported HAE attack) subset participants were included in this arm.

Subject analysis set title	Treatment Period B: Non-HAE
Subject analysis set type	Safety analysis

Subject analysis set description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks or lanadelumab 300 mg solution, SC, q4w for 26 weeks in Treatment Period B if well tolerated (attack-free) for 26 consecutive weeks with lanadelumab treatment during Treatment Period A. Non-HAE attack (subset identified in CRF as not reported HAE attack) subset participants were included in this arm.

Subject analysis set title	Treatment Period B: HAE
Subject analysis set type	Safety analysis

Subject analysis set description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks or lanadelumab 300 mg solution, SC, q4w for 26 weeks in Treatment Period B if well tolerated (attack-free) for 26 consecutive weeks with lanadelumab

treatment during Treatment Period A. HAE attack (subset of AEs identified in CRF as reported HAE attack) subset participants were included in this arm.

Subject analysis set title	Safety Follow-up Period: Non-HAE
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who completed the lanadelumab 300 mg regimen in Treatment Period B returned on Day 378 (for participants who chose to roll over into study TAK-743-5007 [NCT04687137]) or Day 392 as follow-up visit for final assessment in the Safety Follow-up Period. Non-HAE attack (subset identified in CRF as not reported HAE attack) subset participants were included in this arm.

Subject analysis set title	Safety Follow-up Period: HAE
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who completed the lanadelumab 300 mg regimen in Treatment Period B returned on Day 378 (for participants who chose to roll over into study TAK-743-5007) or Day 392 as follow-up visit for final assessment in the Safety Follow-up Period. HAE attack (subset of AEs identified in CRF as reported HAE attack) subset participants were included in this arm.

Primary: Number of Participants Achieving Attack-Free Status for the Efficacy Evaluation Period of Day 0 Through Day 182

End point title	Number of Participants Achieving Attack-Free Status for the Efficacy Evaluation Period of Day 0 Through Day 182[1]

End point description:

A participant was considered as attack free during an efficacy evaluation period if the participant had no investigator-confirmed hereditary angioedema (HAE) attacks during that efficacy evaluation period. A HAE attack was defined as the symptoms or signs consistent with an attack in at least 1 of the following locations: peripheral angioedema (cutaneous swelling involving an extremity, the face, neck, torso, and/or genitourinary region), abdominal angioedema (abdominal pain, with or without abdominal distention, nausea, vomiting, or diarrhea), laryngeal angioedema (stridor, dyspnea, difficulty speaking, difficulty swallowing, throat tightening, or swelling of the tongue, palate, uvula, or larynx). Number of participants achieving attack-free status for the efficacy evaluation period of Day 0 through Day 182 were assessed. Full Analysis Set (FAS) included all participants who received at least 1 dose of investigational medicinal product (IMP).

End point type	Primary

End point timeframe:

Day 0 through Day 182

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 statistics was planned to be reported for this endpoint.

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Investigator-Confirmed Hereditary Angioedema (HAE) Attacks During Each of the Efficacy Evaluation Periods

End point title	Number of Investigator-Confirmed Hereditary Angioedema (HAE) Attacks During Each of the Efficacy Evaluation Periods

End point description:

Efficacy evaluation period consisted of four periods: Day 0 (after study drug administration) through Day 182 (the end of Treatment Period A), Day 0 (after study drug administration) through Day 364 (the end of Treatment Period B), presumed steady-state period from Day 70 through Day 182, presumed steady-state period from Day 70 through Day 364. Number of investigator-confirmed HAE attacks during each of the efficacy evaluation periods were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: HAE attacks				
Day 0 Through Day 182	92			
Day 0 Through Day 364	189			
Day 70 Through Day 182	55			
Day 70 Through Day 364	152			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Investigator-Confirmed Hereditary Angioedema (HAE) Attacks Requiring Acute Treatment During Each of the Efficacy Evaluation Periods

End point title	Number of Investigator-Confirmed Hereditary Angioedema (HAE) Attacks Requiring Acute Treatment During Each of the Efficacy Evaluation Periods

End point description:

Efficacy evaluation period consisted of four periods: Day 0 (after study drug administration) through Day 182 (the end of Treatment Period A), Day 0 (after study drug administration) through Day 364 (the end of Treatment Period B), presumed steady-state period from Day 70 through Day 182, presumed steady-state period from Day 70 through Day 364. Number of investigator-confirmed HAE attacks requiring acute treatment during each of the efficacy evaluation periods were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: HAE attacks				
Day 0 Through Day 182	79			
Day 0 Through Day 364	168			
Day 70 Through Day 182	46			
Day 70 Through Day 364	135			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Moderate or Severe Investigator-Confirmed Hereditary Angioedema (HAE) Attacks During Each of the Efficacy Evaluation Periods

End point title	Number of Moderate or Severe Investigator-Confirmed Hereditary Angioedema (HAE) Attacks During Each of the Efficacy Evaluation Periods

End point description:

Severe attack was defined as Grade 3 (some assistance usually required, medical intervention/therapy required, hospitalizations possible), moderate attack was defined as Grade 2 (some assistance may be needed, no or minimal medical intervention/therapy required). Number of investigator-confirmed moderate or severe HAE attacks during the each of efficacy evaluation periods was assessed. Efficacy evaluation period consisted of four periods: Day 0 (after study drug administration) through Day 182 (the end of Treatment Period A), Day 0 (after study drug administration) through Day 364 (the end of Treatment Period B), presumed steady-state period from Day 70 through Day 182, presumed steady-state period from Day 70 through Day 364. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: HAE attacks				
Day 0 Through Day 182	72			
Day 0 Through Day 364	153			
Day 70 Through Day 182	41			
Day 70 Through Day 364	122			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Maximum Hereditary Angioedema (HAE) Attack Severity During Each of the Efficacy Evaluation Periods

End point title	Number of Participants with Maximum Hereditary Angioedema (HAE) Attack Severity During Each of the Efficacy Evaluation Periods

End point description:

Efficacy evaluation period consisted of four periods: Day 0 (after study drug administration) through Day 182 (the end of Treatment Period A), Day 0 (after study drug administration) through Day 364 (the end of Treatment Period B), presumed steady-state period from Day 70 through Day 182, presumed steady-state period from Day 70 through Day 364. Number of participants with maximum HAE attack severity during each of the efficacy evaluation periods was assessed. HAE attack severity was calculated per participant based on the severity categories as follows: No attack, Mild, Moderate, and Severe. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants				
Day 0 Through Day 182: No Attack	5			
Day 0 Through Day 182: Mild	2			
Day 0 Through Day 182: Moderate	4			
Day 0 Through Day 182: Severe	1			
Day 0 Through Day 364: No Attack	2			
Day 0 Through Day 364: Mild	1			
Day 0 Through Day 364: Moderate	8			
Day 0 Through Day 364: Severe	1			
Day 70 Through Day 182: No Attack	5			
Day 70 Through Day 182: Mild	4			
Day 70 Through Day 182: Moderate	2			
Day 70 Through Day 182: Severe	1			
Day 70 Through Day 364: No Attack	2			
Day 70 Through Day 364: Mild	2			
Day 70 Through Day 364: Moderate	7			
Day 70 Through Day 364: Severe	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of High-Morbidity Investigator-Confirmed Hereditary Angioedema (HAE) Attacks During Each of the Efficacy Evaluation Periods

End point title	Number of High-Morbidity Investigator-Confirmed Hereditary

	Angioedema (HAE) Attacks During Each of the Efficacy Evaluation Periods

End point description:

A high morbidity HAE attack was defined as any attack that has at least 1 of the following characteristics: severe, results in hospitalization (except hospitalization for observation <24 hours), hemodynamically significant (systolic blood pressure <90, requires intravenous (IV) hydration, or associated with syncope or near syncope) or laryngeal. Number of high-morbidity investigator-confirmed HAE attacks during each of the 4 efficacy evaluation periods (Treatment Period A, Overall Treatment Period, Presumed Steady-state Period for Treatment Period A and Overall Presumed Steady-state Period) were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: HAE attacks				
Day 0 Through Day 182	5			
Day 0 Through Day 364	11			
Day 70 Through Day 182	4			
Day 70 Through Day 364	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Hereditary Angioedema (HAE) Attack After Day 0 for the Efficacy Evaluation Period

End point title	Time to First Hereditary Angioedema (HAE) Attack After Day 0 for the Efficacy Evaluation Period

End point description:

The time to the first HAE attack (days) after Day 0 for the efficacy evaluation period of Day 0 through Day 182 was calculated from the date and time of the first dose of lanadelumab for the efficacy evaluation period (Day 0 through Day 182) to the date and time of the first in HAE attack after the first open-label dose for the efficacy evaluation period of Day 0 through Day 182. Kaplan-Meier Method was used for analysis and the Kaplan Meier estimate expressed as time (in days) to first HAE attack After Day 0 for Treatment Period A (Day 0 through Day 182) is presented. FAS included all participants who received at least 1 dose of IMP. 99999= The upper limit of 95% confidence interval (CI) was not evaluable due to low number of participants with events.

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: days				
median (confidence interval 95%)	97.2 (4.2 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Hereditary Angioedema (HAE) Attack After Day 0 for the Efficacy Evaluation Period

End point title	Time to First Hereditary Angioedema (HAE) Attack After Day 0 for the Efficacy Evaluation Period

End point description:

The time to the first HAE attack (days) after Day 0 for the efficacy evaluation period of Day 70 through Day 182 was calculated from the date and time of the first dose of lanadelumab for the efficacy evaluation period (Day 70 through Day 182) to the date and time of the first in HAE attack after the first open-label dose for the efficacy evaluation period of Day 70 through Day 182. Kaplan-Meier Method was used for analysis and the Kaplan Meier estimate expressed as time (in days) to first HAE attack After Day 0 for presumed steady-state period for Treatment Period A (Day 70 through Day 182) is presented. FAS included all participants who received at least 1 dose of IMP. 99999= The upper limit of 95% CI was not evaluable due to low number of participants with events.

End point type	Secondary

End point timeframe:

Day 70 through Day 182

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: days				
median (confidence interval 95%)	91.0 (4.6 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving at Least 50%, 70% and 90% Reduction in the Investigator-Confirmed Normalized Number of Attacks (NNA) per 4 Weeks Relative to the Run-in Period NNA for Each of Efficacy Evaluation Periods

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

	for Each of Efficacy Evaluation Periods

End point description:

Run- in Period was 4 weeks and may have been extended up to 8 weeks to determine participants' Baseline attack rate.period attack rate, multiplied by 100.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants				
Day 0 Through Day 182: ≥50% Reduction	10			
Day 0 Through Day 182: ≥70% Reduction	8			
Day 0 Through Day 182: ≥90% Reduction	6			
Day 0 Through Day 364: ≥50% Reduction	10			
Day 0 Through Day 364: ≥70% Reduction	8			
Day 0 Through Day 364: ≥90% Reduction	6			
Day 70 Through Day 182: ≥50% Reduction	11			
Day 70 Through Day 182: ≥70% Reduction	10			
Day 70 Through Day 182: ≥90% Reduction	6			
Day 70 Through Day 364: ≥50% Reduction	10			
Day 70 Through Day 364: ≥70% Reduction	8			
Day 70 Through Day 364: ≥90% Reduction	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving Normalized Number of Attacks (NNA) <1.0 per 4 Weeks, <0.75 per 4 Weeks, <0.50 per 4 Weeks and <0.25 per 4 Weeks for Each of the Efficacy Evaluation Periods

End point title	Number of Participants Achieving Normalized Number of Attacks (NNA) <1.0 per 4 Weeks, <0.75 per 4 Weeks, <0.50 per 4 Weeks and <0.25 per 4 Weeks for Each of the Efficacy Evaluation Periods

End point description:

The NNA (investigator-confirmed) during each efficacy evaluation period was expressed as a monthly (28 days) HAE attack rate. Number of participants achieving NNA <1.0 per 4 weeks, <0.75 per 4 weeks,

<0.50 per 4 weeks, and <0.25 per 4 weeks for each of the 4 efficacy evaluation periods (Treatment Period A, Overall Treatment Period, Presumed Steady-state Period for Treatment Period A, and Overall Presumed Steady-state Period) were assessed. The responder categories were not mutually exclusive, participants may appear in more than one category as applicable based on their HAE attack rate. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants				
Day 0 Through Day 182: <1.0 per Month	9			
Day 0 Through Day 182: <0.75 per Month	9			
Day 0 Through Day 182: <0.50 per Month	6			
Day 0 Through Day 182: <0.25 per Month	6			
Day 0 Through Day 364: <1.0 per Month	9			
Day 0 Through Day 364: <0.75 per Month	8			
Day 0 Through Day 364: <0.50 per Month	7			
Day 0 Through Day 364: <0.25 per Month	6			
Day 70 Through Day 182: <1.0 per Month	9			
Day 70 Through Day 182: <0.75 per Month	9			
Day 70 Through Day 182: <0.50 per Month	8			
Day 70 Through Day 182: <0.25 per Month	6			
Day 70 Through Day 364: <1.0 per Month	9			
Day 70 Through Day 364: <0.75 per Month	8			
Day 70 Through Day 364: <0.50 per Month	7			
Day 70 Through Day 364: <0.25 per Month	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving Attack-Free Status for the Efficacy

Evaluation Period Day 0 Through Day 364, Day 70 Through Day 182, and Day 70 Through Day 364

End point title	Number of Participants Achieving Attack-Free Status for the Efficacy Evaluation Period Day 0 Through Day 364, Day 70 Through Day 182, and Day 70 Through Day 364

End point description:

A participant was considered as attack free during an efficacy evaluation period if the participant had no investigator-confirmed HAE attacks during that efficacy evaluation period. A HAE attack was defined as the symptoms or signs consistent with an attack in at least 1 of the following locations: peripheral angioedema (cutaneous swelling involving an extremity, the face, neck, torso, and/or genitourinary region), abdominal angioedema (abdominal pain, with or without abdominal distention, nausea, vomiting, or diarrhea), laryngeal angioedema (stridor, dyspnea, difficulty speaking, difficulty swallowing, throat tightening, or swelling of the tongue, palate, uvula, or larynx). Number of participants achieving attack-free status for the 4 efficacy evaluation periods (Overall Treatment Period, Presumed Steady-state Period for Treatment Period A, and Overall Presumed Steady-state Period) were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 364, Day 70 through Day 182, and Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: participants				
Day 0 Through Day 364	2			
Day 70 Through Day 182	5			
Day 70 Through Day 364	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving Attack-Free Status for Monthly Increments

End point title	Number of Participants Achieving Attack-Free Status for Monthly Increments

End point description:

A participant was considered as attack free during an efficacy evaluation period if the participant had no investigator-confirmed HAE attacks during that efficacy evaluation period. A HAE attack was defined as the symptoms or signs consistent with an attack in at least 1 of the following locations: peripheral angioedema (cutaneous swelling involving an extremity, the face, neck, torso, and/or genitourinary region), abdominal angioedema (abdominal pain, with or without abdominal distention, nausea, vomiting, or diarrhea), laryngeal angioedema (stridor, dyspnea, difficulty speaking, difficulty swallowing, throat tightening, or swelling of the tongue, palate, uvula, or larynx). FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

At Months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 and 13

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants				
Month 1	7			
Month 2	8			
Month 3	9			
Month 4	7			
Month 5	9			
Month 6	7			
Month 7	8			
Month 8	6			
Month 9	7			
Month 10	9			
Month 11	8			
Month 12	7			
Month 13	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Attack Free Days During Each of the Efficacy Evaluation Periods

End point title	Percentage of Attack Free Days During Each of the Efficacy Evaluation Periods

End point description:

An attack-free day was defined as a calendar day with no investigator-confirmed HAE attack. HAE attack free days were calculated by counting the number of days in the efficacy evaluation period without an HAE attack and dividing by the number of days the participant contributed to the efficacy evaluation period. Percentage of investigator-confirmed HAE attack free days during each of the efficacy evaluation periods (Treatment Period A, Overall Treatment Period, Presumed Steady-state Period for Treatment Period A, and Overall Presumed Steady-state Period) were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182, Day 0 through Day 364, Day 70 through Day 182, Day 70 through Day 364

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percentage of attack-free days				
arithmetic mean (standard deviation)				
Day 0 Through Day 182	88.53 (± 27.146)			
Day 0 Through Day 364	89.04 (± 27.015)			
Day 70 Through Day 182	90.34 (± 21.952)			
Day 70 Through Day 364	89.85 (± 25.015)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Achieving Investigator-Confirmed Hereditary Angioedema (HAE) Attack-Free Intervals

End point title	Number of Participants Achieving Investigator-Confirmed Hereditary Angioedema (HAE) Attack-Free Intervals

End point description:

A participant was considered as attack free during a time period if the participant had no investigator-confirmed HAE attacks during that time period. Participants who discontinued during a time period were considered as non-responders for that time period. Number of participants achieving investigator-confirmed HAE attack free intervals from Day 0 through Day 182 were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Day 0 through Day 182

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment Emergent Adverse Events (TEAEs) Including Adverse Events of Special Interest (AESI) and Serious Adverse Events (SAEs)

End point title	Number of Participants with Treatment Emergent Adverse Events (TEAEs) Including Adverse Events of Special Interest (AESI) and Serious Adverse Events (SAEs)

End point description:

TEAE=any event emerging at or after initiation of treatment with investigational product (IP) or any existing event that worsens in intensity/frequency on exposure to IP. Serious TEAE=any untoward clinical manifestation of signs, symptoms, outcomes (related to IP or not) at any dose: results in death, was life-threatening, requires inpatient/prolongation of hospitalization, resulted in persistent/significant disability/incapacity, congenital abnormality/birth defect, important medical event. AESI=investigator-reported hypersensitivity reactions, events of disordered coagulation as bleeding/hypercoagulable AESI. Adverse events (AEs) were classified as HAE attack and non-HAE attack reported AEs and are categorized accordingly. As Pre-specified in the protocol, TEAEs, SAEs and AESIs were collected per Period i.e., Treatment Period A, B and Safety follow-up Period and data is reported accordingly. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

From first dose of the study drug up to end of study (EOS) (up to Day 392)

End point values	Treatment Period A: Non-HAE	Treatment Period A: HAE	Treatment Period B: Non-HAE	Treatment Period B: HAE
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: participants				
Any TEAEs	10	8	9	8
AESI	3	0	0	0
Any Serious TEAEs	1	1	1	0

End point values	Safety Follow-up Period: Non-HAE	Safety Follow-up Period: HAE		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: participants				
Any TEAEs	0	3		
AESI	0	0		
Any Serious TEAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Lanadelumab

End point title	Plasma Concentrations of Lanadelumab

End point description:

Pharmacokinetic (PK) Set included all participants in the FAS who had at least 1 evaluable post dose PK concentration value. n= number analysed indicates the number of participants with data available for analysis at a specific time point.

End point type	Secondary

End point timeframe:

Predose on Days 0, 56, 98, 140, 182, 266, 350, 364, and at any time on Day 378 or 392

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 0 (n=12)	25.584 (± 50.2034)			
Day 56 (n=12)	23630.973 (± 8665.1099)			
Day 98 (n=12)	24142.776 (± 9575.7596)			
Day 140 (n=11)	24613.885 (± 9319.6672)			
Day 182 (n=12)	23679.526 (± 6793.3003)			
Day 266 (n=12)	19269.249 (± 8870.0355)			
Day 350 (n=3)	13225.533 (± 2538.8239)			
Day 364 (n=10)	22329.820 (± 7527.7165)			
Day 378/392 (n=12)	19308.033 (± 7708.1882)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Angioedema Quality of Life (AE-QoL) Questionnaire Total Score

End point title	Change From Baseline in Angioedema Quality of Life (AE-QoL) Questionnaire Total Score

End point description:

The AE-QoL questionnaire is a self-administered validated instrument to assess health related (HR)QoL among participants with recurrent angioedema (including HAE). The AE-QoL consists of 17 disease-specific quality-of-life items, to produce a total AE-QoL score and 4 domain scores (functioning, fatigue/mood, fear/shame, and nutrition) and each of the 17 items had a five-point response scale ranging from 1 (Never) to 5 (Very Often). The questionnaire was scored according to the developers' guidelines to produce 4 domain scores (functioning, fatigue/mood, fear/shame, nutrition) yielding a total score. The raw total score (mean of all item scores) was rescaled using linear transformations into final percentage scores ranging 0 to 100, based on the maximum possible score, where higher the score, greater the QoL impairment. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

Days 0, 28, 56, 98, 126, 154, 182, 266, 364, 378 or 392

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: score on a scale				
arithmetic mean (standard deviation)				
Day 0	46.57 (± 20.885)			
Day 28	26.35 (± 31.129)			
Day 56	28.43 (± 28.255)			
Day 98	26.96 (± 30.926)			
Day 126	32.60 (± 33.999)			
Day 154	21.69 (± 28.750)			
Day 182	26.10 (± 33.978)			
Day 266	26.96 (± 29.951)			
Day 364	26.59 (± 34.428)			
Day 378/392	28.55 (± 31.934)			

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 biomarker cleaved high molecular weight kininogen (cHMWK) level to assess pharmacodynamics (PD) of lanadelumab. Pharmacodynamic (PD) Set included all participants in the FAS who had at least 1 evaluable post dose PD value. n= number analysed indicates the number of participants with data available for analysis at the given time point.

End point type	Secondary

End point timeframe:

Predose on Days 0, 56, 98, 140, 182, 266, 350, 364, and at any time on Day 378 or 392

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percentage of cHMWK				
arithmetic mean (standard deviation)				
Day 0 (n=12)	63.04 (± 22.096)			
Day 56 (n=12)	30.88 (± 17.090)			
Day 98 (n=12)	32.40 (± 18.829)			
Day 140 (n=11)	35.67 (± 13.787)			
Day 182 (n=12)	30.31 (± 17.344)			
Day 266 (n=12)	21.69 (± 11.221)			
Day 350 (n=3)	39.83 (± 12.407)			
Day 364 (n=10)	27.51 (± 12.901)			
Day 378/392 (n=12)	40.65 (± 15.828)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-drug Antibody (ADA) in Plasma

End point title	Number of Participants With Positive Anti-drug Antibody (ADA) in Plasma

End point description:

Baseline was defined as the last non-missing value prior to first dose of study drug (based on date or date/time). FAS included all participants who received at least 1 dose of IMP. n= number analysed indicates the number of participants with data available for analysis at the given time point.

End point type	Secondary

End point timeframe:

Predose on Days 0 (or Baseline), 56, 98, 140, 182, 266, 350, 364, and at any time on Day 378 or 392

End point values	Lanadelumab 300 mg q2w or q4w			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants				
Day 0 [or Baseline] (n=12)	0			
Day 56 (n=12)	0			
Day 98 (n=12)	0			
Day 140 (n=11)	0			

Day 182 (n=12)	0			
Day 266 (n=12)	0			
Day 350 (n=3)	0			
Day 364 (n=10)	0			
Day 378/392 (n=12)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs Related to Clinical Laboratory Tests

End point title	Number of Participants With TEAEs Related to Clinical Laboratory Tests

End point description:

A TEAE was defined as any event emerging or manifesting at or after the initiation of treatment with an IP or medicinal product or any existing event that worsens in either intensity or frequency following exposure to the IP or medicinal product. As Pre-specified in the protocol, the TEAEs were collected per Period i.e., Treatment Period A, B and Safety follow-up Period. The data is reported as per HAE attack and non-HAE attack per Period. Number of participants with TEAEs related to clinical laboratory tests (hematology, clinical chemistry, coagulation, and urinalysis) were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

From first dose of the study drug up to end of study (EOS) (up to Day 392)

End point values	Treatment Period A: Non-HAE	Treatment Period A: HAE	Treatment Period B: Non-HAE	Treatment Period B: HAE
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: participants	0	0	0	0

End point values	Safety Follow-up Period: Non-HAE	Safety Follow-up Period: HAE		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs Related to Vital Signs

End point title	Number of Participants With TEAEs Related to Vital Signs

End point description:

A TEAE was defined as any event emerging or manifesting at or after the initiation of treatment with an IP or medicinal product or any existing event that worsens in either intensity or frequency following exposure to the IP or medicinal product. As Pre-specified in the protocol, the TEAEs were collected per Period i.e., Treatment Period A, B and Safety follow-up Period. The data is reported as per HAE attack and non-HAE attack per Period. Number of participants with TEAEs related to vital signs (blood pressure (BP), heart rate (HR), body temperature, and respiratory rate) were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

From first dose of the study drug up to end of study (EOS) (up to Day 392)

End point values	Treatment Period A: Non-HAE	Treatment Period A: HAE	Treatment Period B: Non-HAE	Treatment Period B: HAE
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: participants	0	0	0	0

End point values	Safety Follow-up Period: Non-HAE	Safety Follow-up Period: HAE		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs Related to Electrocardiogram (ECG)

End point title	Number of Participants With TEAEs Related to Electrocardiogram (ECG)

End point description:

A TEAE was defined as any event emerging or manifesting at or after the initiation of treatment with an IP or medicinal product or any existing event that worsens in either intensity or frequency following exposure to the IP or medicinal product. As Pre-specified in the protocol, the TEAEs were collected per Period i.e., Treatment Period A, B and Safety follow-up Period. The data is reported as per HAE attack and non-HAE attack per Period. Number of participants with TEAEs related to 12 lead-ECG were assessed. FAS included all participants who received at least 1 dose of IMP.

End point type	Secondary

End point timeframe:

From first dose of the study drug up to end of study (EOS) (up to Day 392)

End point values	Treatment Period A: Non-HAE	Treatment Period A: HAE	Treatment Period B: Non-HAE	Treatment Period B: HAE
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	12	12
Units: participants	0	0	0	0

End point values	Safety Follow-up Period: Non-HAE	Safety Follow-up Period: HAE		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	12		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of the study drug up to end of study (EOS) (up to Day 392)

Adverse event reporting additional description:

FAS included all participants who received at least 1 dose of IMP. As Pre-specified in the protocol, the TEAEs were collected per Period i.e., Treatment Period A, B and Safety follow-up Period. The data is reported as per HAE attack and non-HAE attack per Period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Treatment Period A: Non-HAE

Reporting group description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks in Treatment Period A. Non-HAE attack (subset identified in case report form [CRF] as not reported HAE attack) subset participants were included in this arm.

Reporting group title	Treatment Period A: HAE

Reporting group description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks in Treatment Period A. HAE attack (subset of AEs identified in CRF as reported HAE attack) subset participants were included in this arm.

Reporting group title	Treatment Period B: Non-HAE

Reporting group description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks or lanadelumab 300 mg solution, SC, q4w for 26 weeks in Treatment Period B if well tolerated (attack-free) for 26 consecutive weeks with lanadelumab treatment during Treatment Period A. Non-HAE attack (subset identified in CRF as not reported HAE attack) subset participants were included in this arm.

Reporting group title	Treatment Period B: HAE

Reporting group description:

Lanadelumab 300 mg solution, SC, q2w for 26 weeks or lanadelumab 300 mg solution, SC, q4w for 26 weeks in Treatment Period B if well tolerated (attack-free) for 26 consecutive weeks with lanadelumab treatment during Treatment Period A. HAE attack (subset of AEs identified in CRF as reported HAE attack) subset participants were included in this arm.

Reporting group title	Safety Follow-up Period: Non-HAE

Reporting group description:

Participants who completed the lanadelumab 300 mg regimen in Treatment Period B returned on Day 378 (for participants who chose to roll over into study TAK-743-5007 [NCT04687137]) or Day 392 as follow-up visit for final assessment in the Safety Follow-up Period. Non-HAE attack (subset identified in CRF as not reported HAE attack) subset participants were included in this arm.

Reporting group title	Safety Follow-up Period: HAE

Reporting group description:

Participants who completed the lanadelumab 300 mg regimen in Treatment Period B returned on Day 378 (for participants who chose to roll over into study TAK-743-5007) or Day 392 as follow-up visit for final assessment in the Safety Follow-up Period. HAE attack (subset of AEs identified in CRF as reported HAE attack) subset participants were included in this arm.

Serious adverse events	Treatment Period A: Non-HAE	Treatment Period A: HAE	Treatment Period B: Non-HAE
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	1 / 12 (8.33%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 12 (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
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (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
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment Period B: HAE	Safety Follow-up Period: Non-HAE	Safety Follow-up Period: HAE
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Treatment Period A: Non-HAE	Treatment Period A: HAE	Treatment Period B: Non-HAE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)	7 / 12 (58.33%)	9 / 12 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma	Additional description: Number of participants at risk in each arm is based on the female population in this study.		
subjects affected / exposed[1]	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	6 / 12 (50.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	37	0	0
Injection site erythema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	4	0	5
Injection site pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Infusion site pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injection site pain			

subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Injection site swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Allergy to chemicals			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anaphylactic shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Contrast media allergy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Drug hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea	Additional description: Number of participants at risk in each arm is based on the female population in this study.		
subjects affected / exposed[2]	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Anxiety disorder			

subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Heat illness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Thermal burn			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Tooth fracture			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	0 / 12 (0.00%)	7 / 12 (58.33%)	0 / 12 (0.00%)
occurrences (all)	0	92	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	12	0	9
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	8	0	5

Hypoaesthesia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Intercostal neuralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dental caries			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hyperaesthesia teeth			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Large intestine polyp			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	10	0	10
Toothache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Alopecia areata			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Angioedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eczema asteatotic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Back pain			

subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Infections and infestations			
Cystitis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Furuncle			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Laryngopharyngitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	2
Oral herpes			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vulvitis	Additional description: Number of participants at risk in each arm is based on the female population in this study.		
subjects affected / exposed[3]	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			

subjects affected / exposed	1 / 12 (8.33%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Treatment Period B: HAE	Safety Follow-up Period: Non-HAE	Safety Follow-up Period: HAE
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 12 (66.67%)	0 / 12 (0.00%)	3 / 12 (25.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma	Additional description: Number of participants at risk in each arm is based on the female population in this study.		
subjects affected / exposed[1]	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infusion site pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injection site swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Malaise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to chemicals			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Anaphylactic shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Contrast media allergy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea	Additional description: Number of participants at risk in each arm is based on the female population in this study.		
subjects affected / exposed[2]	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fall			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Heat illness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	8 / 12 (66.67%)	0 / 12 (0.00%)	3 / 12 (25.00%)
occurrences (all)	97	0	11
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Intercostal neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyperaesthesia teeth			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Large intestine polyp			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia areata			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Angioedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eczema asteatotic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

Cystitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Laryngopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vulvitis	Additional description: Number of participants at risk in each arm is based on the female population in this study.		
subjects affected / exposed[3]	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Number of subjects exposed to this adverse event is based on the female population in this study.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event is based on the female population in this study.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event is based on the female population in this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 July 2019	The changes implemented based on Amendment 1 were: -Added the requirement to exclude participants with a known hypersensitivity to the IMP or its components as a new exclusion criterion. -Corrected text regarding the number of days for reporting non-serious AEs that are reported as HAE attacks for consistency.
05 October 2020	The changes implemented based on Amendment 2 were: -Revised Sponsor approval -Added that participants may elect to roll over into an expanded access study (Study TAK-743-5007). -Revised interim analysis to include 2 interim analyses: first analysis was to be performed when the first 6 participants enrolled in the study had reached Day 182 or discontinued in Treatment Period A (26 weeks of treatment) and second analysis was to be performed when the first 4 participants enrolled in the study had reached Day 364 or discontinued. -Corrected error that screening visit was also Visit 1. -Corrected error on collection of prior treatment to reflect that prior treatments should be collected prior to screening visit. -Corrected investigator-confirmed HAE attacks to state: 3 or more than 3 investigator-confirmed HAE attacks. -Removed body weight from physical exams at Visit 26 and Visit 27. -Removed pregnancy tests at Visit 26 and Visit 27. -Removed following sentence: Overall attack rates will be estimated using a Poisson general linear model adjusting for run-in period attack rate and accounting for potential overdispersion. -Added 'if applicable' to analysis of efficacy endpoints at 4 efficacy evaluation periods. -Other efficacy endpoints along with statistical methods for their analysis were added. -Added language that subgroup analyses may be performed. -Corrected carbon dioxide to bicarbonate.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported