EU Clinical Trials Register

Clinical trial results:

An open-label, single-arm, non-randomized phase 3 study to evaluate clinical efficacy, safety, and pharmacokinetics of subcutaneous administration of human plasma-derived C1-esterase inhibitor in the prophylactic treatment of hereditary angioedema in Japanese subjects

Summary

EudraCT number	2019-003921-99
Trial protocol	Outside EU/EEA
Global end of trial date	22 February 2021

Results information

Result version number	v1 (current)
This version publication date	01 September 2021
First version publication date	01 September 2021

Trial information

Trial identification

Sponsor protocol code	CSL830_3003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CSL Behring K.K.
Sponsor organisation address	1-2-3-Kita Aoyama, Minato-ku, Tokyo, Japan, 107-0061
Public contact	Trial Registration Coordinator, CSL Behring K.K., +1 610878-4000, clinicaltrials@cslbehring.com
Scientific contact	Trial Registration Coordinator, CSL Behring K.K., +1 610878-4000, clinicaltrials@cslbehring.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	02 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are to evaluate the clinical efficacy and pharmacokinetics of subcutaneous (SC) CSL830 in the prophylactic treatment of hereditary angioedema (HAE) in Japanese subjects.

Protection of trial subjects:

This study was carried out in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines and standard operating procedures for clinical research and development at CSL Behring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 June 2020
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: 9
Worldwide total number of subjects	9
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)	8
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects will enter into a Run-in Period to evaluate their underlying HAE disease status and their HAE attack rate. Subjects must
experience ≥ 4 HAE attacks within any 2 consecutive months within the 3-months prior to Screening to be eligible to proceed to Screening.

Period 1

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

Arms

Arm title	CSL830

Arm description:

Powder and solvent for solution for injection for Subcutaneous use

Arm type	Experimental
Investigational medicinal product name	C1-esterase inhibitor (C1-INH)
Investigational medicinal product code	
Other name	CSL830, Berinert
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single SC injection of 60 IU/kg CSL830 twice per week for up to 16 weeks.

Number of subjects in period 1	CSL830
Started	9
Completed	9

Baseline characteristics

Reporting groups

Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	9	9	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	8	8	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	37.9		
standard deviation	± 11.43	-	
Gender categorical			
Units: Subjects			
Female	6	6	
Male	3	3	

End points

End points reporting groups

Reporting group title	CSL830
Reporting group description:	
Powder and solvent for solution for injection for Subcutaneous use	

Primary: Time-normalized number of HAE attacks during treatment with CSL830

End point title	Time-normalized number of HAE attacks during treatment with CSL830[1]
End point description:	

End point type	Primary
End point timeframe:	
Up to 14 weeks	

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: Descriptive statistics were used as this is a single-arm study.

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Number of HAE attacks per month				
arithmetic mean (standard deviation)				
Baseline (run-in period)	3.691 (± 1.0909)			
CSL830 Treatment Period	0.295 (± 0.4815)			

Statistical analyses

No statistical analyses for this end point

Primary: Trough concentration of C1-INH functional activity

End point title	Trough concentration of C1-INH functional activity[2]
End point description:	

End point type	Primary
End point timeframe:	
Up to 10-14 days after the last dose at Week 16	

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: Descriptive statistics were used as this is a single-arm study.

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
arithmetic mean (standard deviation)	59.77 (± 19.527)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the concentration curve (AUC) for C1-INH functional activity

End point title	Area under the concentration curve (AUC) for C1-INH functional activity[3]
End point description:	

End point type	Primary

End point timeframe:

Up to 10-14 days after the last dose on Week 16

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: Descriptive statistics were used as this is a single-arm study.

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: h*%				
arithmetic mean (standard deviation)				
AUC (0-tau)	5317.1164 (± 1347.7965)			
AUC (0-last)	13091.4870 (± 3835.3917)			

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of subjects who achieved ≥ 90%, ≥ 70%, and ≥ 50% relative reduction in time-normalized monthly HAE attack rate

End point title	The percentage of subjects who achieved ≥ 90%, ≥ 70%, and ≥ 50% relative reduction in time-normalized monthly HAE attack rate
End point description:	

End point type	Secondary

End point timeframe:

Up to 14 weeks

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent reduction in monthly HAE attacks				
number (confidence interval 95%)				
Reduction of >= 50%	100.0 (70.1 to 100.0)			
Reduction of >= 70%	77.8 (45.3 to 93.7)			
Reduction of >= 90%	66.7 (35.4 to 87.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: The relative reduction in the time-normalized number of rescue medication uses per month for treatment of HAE attacks

End point title	The relative reduction in the time-normalized number of rescue medication uses per month for treatment of HAE attacks

End point description:

End point type	Secondary

End point timeframe:

Up to 14 weeks

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
arithmetic mean (standard deviation)	84.980 (± 25.3320)			

Statistical analyses

No statistical analyses for this end point

Secondary: The number of reported adverse events (AEs)

End point title	The number of reported adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

Up to 18 weeks

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: number of AEs				
number (not applicable)				
Number of subjects reporting AEs	7			
Number of AEs	109			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects reporting AEs and injection site reactions that began within 24 hours of CSL830 administration

End point title	Percentage of subjects reporting AEs and injection site reactions that began within 24 hours of CSL830 administration

End point description:

End point type	Secondary

End point timeframe:

Up to 24 hours after dose of CSL830

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent of subjects				
number (not applicable)				
AEs	66.7			
Injection site reactions	33.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean trough C1-INH functional activity during treatment with CSL830

End point title	Mean trough C1-INH functional activity during treatment with CSL830
End point description:	
End point type	Secondary
End point timeframe:	
Up to 16 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent functional activity				
arithmetic mean (standard deviation)				
week 3	74.37 (± 12.719)			
week 7	66.32 (± 21.647)			
week 11	67.04 (± 18.471)			
week 16	59.77 (± 19.527)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean C1-INH antigen levels during treatment with CSL830

End point title	Mean C1-INH antigen levels during treatment with CSL830
End point description:	
End point type	Secondary
End point timeframe:	
Up to 16 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mg/mL				
arithmetic mean (standard deviation)				
week 3	0.2076 (± 0.1431)			
week 7	0.1957 (± 0.1639)			
week 11	0.2102 (± 0.1909)			

week 16	0.1857 (± 0.1503)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean C4 antigen levels during treatment with CSL830

End point title	Mean C4 antigen levels during treatment with CSL830
End point description:	

End point type	Secondary
End point timeframe:	
Up to 16 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: mg/dL				
arithmetic mean (standard deviation)				
week 3	17.721 (± 6.2850)			
week 7	16.259 (± 6.8515)			
week 11	17.992 (± 6.3218)			
week 16	15.716 (± 7.6020)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from week 1 in Subject-reported Angioedema Quality of Life (AEQoL) total score at week 16

End point title	Change from week 1 in Subject-reported Angioedema Quality of Life (AEQoL) total score at week 16
End point description:	

End point type	Secondary
End point timeframe:	
Week 1 and Week 16	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
arithmetic mean (standard deviation)	-24.020 (± 22.9006)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subject-reported Global Assessments of Reponse to Therapy outcomes (SGART)

End point title	Subject-reported Global Assessments of Reponse to Therapy outcomes (SGART)
End point description:	

End point type	Secondary
End point timeframe:	
Up to 16 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent of subjects				
number (not applicable)				
Good	33.3			
Excellent	66.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-reported Global Assessments of Reponse to Therapy outcomes (IGART)

End point title	Investigator-reported Global Assessments of Reponse to Therapy outcomes (IGART)
End point description:	

End point type	Secondary

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent of subjects				
number (not applicable)				
Good	11.1			
Excellent	88.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Absolute Reduction in Time-normalized Number of HAE Attacks per Month

End point title	Mean Absolute Reduction in Time-normalized Number of HAE Attacks per Month
End point description:	

End point type	Secondary
End point timeframe:	
up to 14 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Number of HAE attacks				
arithmetic mean (standard deviation)	-3.396 (± 1.3788)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Absolute Reduction in Time-normalized Number of HAE Attacks per Month

End point title	Median Absolute Reduction in Time-normalized Number of HAE Attacks per Month
End point description:	

End point type	Secondary
End point timeframe:	
up to 14 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Number of HAE attacks				
median (inter-quartile range (Q1-Q3))	-3.581 (-4.348 to -2.899)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Relative Reduction in Time-normalized Number of HAE Attacks per Month

End point title	Mean Relative Reduction in Time-normalized Number of HAE Attacks per Month
End point description:	

End point type	Secondary
End point timeframe:	
up to 14 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
arithmetic mean (standard deviation)	89.310 (± 18.0156)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Relative Reduction in Time-normalized Number of HAE Attacks per Month

End point title	Median Relative Reduction in Time-normalized Number of HAE Attacks per Month
End point description:	

End point type	Secondary
End point timeframe:	
up to 14 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: percent				
median (inter-quartile range (Q1-Q3))	100.0 (84.946 to 100.000)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Relative Reduction in Time-normalized Number of Moderate or Severe HAE Attacks per Month

End point title	Mean Relative Reduction in Time-normalized Number of Moderate or Severe HAE Attacks per Month
End point description:	

End point type	Secondary
End point timeframe:	
Up to 14 weeks	

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percent				
arithmetic mean (standard deviation)	88.841 (± 16.0551)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Relative Reduction in Time-normalized Number of Moderate or Severe HAE Attacks per Month

End point title	Median Relative Reduction in Time-normalized Number of Moderate or Severe HAE Attacks per Month
End point description:	

End point type	Secondary

End point timeframe:

Up to 14 weeks

End point values	CSL830			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percent				
median (inter-quartile range (Q1-Q3))	100.0 (73.297 to 100.000)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events: Up to 18 weeks per subject	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	CSL830
Reporting group description: Powder and solvent for solution for injection for Subcutaneous use	

Serious adverse events	CSL830		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	CSL830		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	3		
Injection site erythema			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	25		
Injection site reaction			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	16		
Malaise			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	19		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	30		
Urticaria			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	4		
Blister			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 9 (22.22%)		
occurrences (all)	2		
Acute sinusitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Otitis media			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2019	-Modified rescue therapy to include only therapies approved in Japan. - Adjustments to clarify women of childbearing potential and contraception in Japan. - Added Appendix 2 for reporting of HAE attacks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported