Clinical trial results:
A multicenter, randomized, placebo-controlled, parallel-arm study to investigate the efficacy, pharmacokinetics, and safety of CSL312 in subjects with hereditary angioedema

Summary

EudraCT number	2018-000605-24
Trial protocol	DE
Global end of trial date	15 October 2021

Results information

Result version number	v1 (current)
This version publication date	29 October 2022
First version publication date	29 October 2022

Trial information

Trial identification

Sponsor protocol code	CSL312_2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03712228
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring LLC
Sponsor organisation address	1020 First Avenue, King of Prussia, United States, 19406
Public contact	Trial Registration Coordinator, CSL Behring LLC, +1 610 878 4000, clinicaltrials@cslbehring.com
Scientific contact	Trial Registration Coordinator, CSL Behring LLC, +1 610 878 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 December 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 October 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to evaluate the efficacy of CSL312 in the prevention of HAE attacks in subjects with C1-INH HAE.

Protection of trial subjects:

Standard of care

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 October 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	United States: 11
Worldwide total number of subjects	44
EEA total number of subjects	17

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)	0
Adults (18-64 years)	43
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Treatment Period 1 participants were assigned to 1 of 5 treatment arms. Treatment period 2 participants that completed Treatment Period 1 were assigned to either CSL312 (medium) or CSL312 (high) and could be up-titrated from CSL312 (medium) to CSL312 (med/high), if necessary. They were down-titrated from CSL312 (high) to CSL312 (medium). Only 2 sub

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects with C1-INH HAE receiving buffer only.

Placebo: Buffer without active ingredient.

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

Dosage and administration details:

Subjects with C1-INH HAE receiving buffer only.

Placebo: Buffer without active ingredient.

Arm title	CSL312 (low)

Arm description:

Subjects with C1-INH HAE receiving low dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects with C1-INH HAE receiving low dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm title	CSL312 (med)

Arm description:

Subjects with C1-INH HAE receiving medium dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects with C1-INH HAE receiving medium dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm title	CSL312 (high)

Arm description:

Subjects with C1-INH HAE receiving high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects with C1-INH HAE receiving high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm title	CSL312 (med/high)

Arm description:

Subjects with C1-INH HAE receiving medium/high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects with C1-INH HAE receiving medium/high dose CSL312

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use

Arm title	CSL312 (FXII/PLG HAE)

Arm description:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312

Arm type	Experimental

Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312

Number of subjects in period 1	Placebo	CSL312 (low)	CSL312 (med)
Started	8	9	8
Completed	8	9	8
Not completed	0	0	0
Lack of efficacy	-	-	-

Number of subjects in period 1	CSL312 (high)	CSL312 (med/high)	CSL312 (FXII/PLG HAE)
Started	7	6	6
Completed	7	6	5
Not completed	0	0	1
Lack of efficacy	-	-	1

Period 2

Period 2 title	Treatment Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CSL312 (med)

Arm description:

Subjects with C1-INH HAE receiving medium dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects with C1-INH HAE receiving medium dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous

and subcutaneous use.

Arm title	CSL312 (high)

Arm description:

Subjects with C1-INH HAE receiving high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects with C1-INH HAE receiving high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Arm title	CSL312 (FXII/PLG HAE)

Arm description:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312.

Number of subjects in period 2[1]	CSL312 (med)	CSL312 (high)	CSL312 (FXII/PLG HAE)
Started	20	18	2
Completed	20	16	2
Not completed	0	2	0
Consent withdrawn by subject	-	1	-
Pregnancy	-	1	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only 2 subjects from the CSL312 (FXII/PLG HAE) arm were treated with CSL312 in Treatment Period 2.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects with C1-INH HAE receiving buffer only. Placebo: Buffer without active ingredient.	
Reporting group title	CSL312 (low)
Reporting group description:	
Subjects with C1-INH HAE receiving low dose CSL312. Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.	
Reporting group title	CSL312 (med)
Reporting group description:	
Subjects with C1-INH HAE receiving medium dose CSL312. Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.	
Reporting group title	CSL312 (high)
Reporting group description:	
Subjects with C1-INH HAE receiving high dose CSL312. Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.	
Reporting group title	CSL312 (med/high)
Reporting group description:	
Subjects with C1-INH HAE receiving medium/high dose CSL312. Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.	
Reporting group title	CSL312 (FXII/PLG HAE)
Reporting group description:	
Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312	

Reporting group values	Placebo	CSL312 (low)	CSL312 (med)
Number of subjects	8	9	8
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	9	8
From 65-84 years	0	0	0
85 years and over	0	0	0

Gender categorical Units: Subjects			
Female	4	7	2
Male	4	2	6

Reporting group values	CSL312 (high)	CSL312 (med/high)	CSL312 (FXII/PLG HAE)
Number of subjects	7	6	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	6	6
From 65-84 years	1	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	5	3	6
Male	2	3	0

Reporting group values	Total		
Number of subjects	44		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	43		
From 65-84 years	1		
85 years and over	0		
Gender categorical Units: Subjects			
Female	27		
Male	17		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects with C1-INH HAE receiving buffer only.

Placebo: Buffer without active ingredient.

Reporting group title	CSL312 (low)

Reporting group description:

Subjects with C1-INH HAE receiving low dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (med)

Reporting group description:

Subjects with C1-INH HAE receiving medium dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (high)

Reporting group description:

Subjects with C1-INH HAE receiving high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (med/high)

Reporting group description:

Subjects with C1-INH HAE receiving medium/high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (FXII/PLG HAE)

Reporting group description:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312

Reporting group title	CSL312 (med)

Reporting group description:

Subjects with C1-INH HAE receiving medium dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (high)

Reporting group description:

Subjects with C1-INH HAE receiving high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (FXII/PLG HAE)

Reporting group description:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312

Primary: The mean Time normalized number of HAE attacks per month in Subjects With C1-INH HAE during Treatment Period 1

End point title	The mean Time normalized number of HAE attacks per month in Subjects With C1-INH HAE during Treatment Period 1[1]

End point description:

The time-normalized number of HAE attacks per month during Treatment Period 1 for a subject was calculated as the (number of HAE attacks / length of subject's evaluation period in days) * 30.4375

End point type	Primary

End point timeframe:

13 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Number of HAE attacks per month				
arithmetic mean (standard deviation)	4.24 (± 1.801)	0.48 (± 1.057)	0.05 (± 0.127)	0.35 (± 0.407)

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of HAE attacks per month				
arithmetic mean (standard deviation)	0.14 (± 0.222)			

Statistical analyses

Statistical analysis title	Dose comparisons
Comparison groups	CSL312 (med) v Placebo
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Dose comparisons
Comparison groups	CSL312 (high) v Placebo

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Dose comparisons
Comparison groups	CSL312 (med) v CSL312 (high)
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.082
Method	Wilcoxon (Mann-Whitney)

Secondary: The number of responder subjects with C1-INH HAE during Treatment Period 1

End point title	The number of responder subjects with C1-INH HAE during Treatment Period 1[2]

End point description:

Response is defined as a ≥ 50% relative reduction in the time-normalized number of HAE attacks (per month) during Treatment Period 1 compared to each subject's time-normalized number of HAE attacks (per month) during the Run-in Period

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Number of participants				
number (not applicable)	0	9	8	6

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of participants				
number (not applicable)	6			

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of responder subjects with C1-INH HAE during Treatment Period 1

End point title	The percentage of responder subjects with C1-INH HAE during Treatment Period 1[3]

End point description:

Response is defined as a ≥ 50% relative reduction in the time-normalized number of HAE attacks (per month) during Treatment Period 1 compared to each subject's time-normalized number of HAE attacks (per month) during the Run-in Period.

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Percentage of participants				
number (not applicable)	0	100	100	85.7

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage of participants				
number (not applicable)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of HAE Attack-free Subjects With C1-INH HAE During Treatment Period 1

End point title	The Number of HAE Attack-free Subjects With C1-INH HAE During Treatment Period 1[4]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Number of participants				
number (not applicable)	0	5	7	3

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of participants				
number (not applicable)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: The percentage of HAE attack-free subjects with C1-INH HAE during Treatment Period 1

End point title	The percentage of HAE attack-free subjects with C1-INH HAE during Treatment Period 1[5]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Percentage of participants				
number (not applicable)	0	55.6	87.5	42.9

End point values	CSL312 (med/high)			

Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage of participants				
number (not applicable)	66.7			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Mild, Moderate or Severe HAE Attacks in Subjects With C1-INH HAE During Treatment Period 1

End point title	The Number of Mild, Moderate or Severe HAE Attacks in Subjects With C1-INH HAE During Treatment Period 1[6]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Number of HAE attacks				
number (not applicable)				
Mild	32	3	0	2
Moderate	43	9	1	4
Severe	20	0	0	1

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of HAE attacks				
number (not applicable)				
Mild	2			
Moderate	0			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Mild, Moderate or Severe HAE Attacks in Subjects With C1-INH HAE During Treatment Period 1

End point title	The Percentage of Mild, Moderate or Severe HAE Attacks in Subjects With C1-INH HAE During Treatment Period 1[7]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Percentage of HAE attacks				
number (not applicable)				
Mild	33.7	25.0	0	28.6
Moderate	45.3	75.0	100	57.1
Severe	21.1	0	0	14.3

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage of HAE attacks				
number (not applicable)				
Mild	100			
Moderate	0			
Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The mean time-normalized number of mild, moderate or severe HAE attacks per month in subjects with C1-INH HAE during Treatment Period 1

End point title	The mean time-normalized number of mild, moderate or severe HAE attacks per month in subjects with C1-INH HAE during Treatment Period 1[8]

End point description:

The time-normalized number of HAE attacks per month during Treatment Period 1 for a subject was calculated as the (number of HAE attacks / length of subject’s evaluation period in days) * 30.4375

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Number of HAE attacks per month				
arithmetic mean (standard deviation)				
Mild	1.42 (± 1.395)	0.12 (± 0.177)	0 (± 0)	0.10 (± 0.168)
Moderate	1.93 (± 1.403)	0.36 (± 1.087)	0.05 (± 0.127)	0.20 (± 0.347)
Severe	0.89 (± 1.365)	0 (± 0)	0 (± 0)	0.05 (± 0.136)

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of HAE attacks per month				
arithmetic mean (standard deviation)				
Mild	0.14 (± 0.222)			
Moderate	0 (± 0)			
Severe	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Subjects with at least one (1) HAE Attack Treated With On-demand HAE Medication, in Subjects With C1-INH HAE During Treatment Period 1

End point title	The Number of Subjects with at least one (1) HAE Attack Treated With On-demand HAE Medication, in Subjects With C1-INH HAE During Treatment Period 1[9]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Number of participants				
number (not applicable)	8	3	1	2

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Subjects with at least one (1) HAE Attack Treated With On-demand HAE Medication, in Subjects With C1-INH HAE During Treatment Period 1

End point title	The Percentage of Subjects with at least one (1) HAE Attack Treated With On-demand HAE Medication, in Subjects With C1-INH HAE During Treatment Period 1[10]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Percentage of participants				
number (not applicable)	100	33.3	12.5	28.6

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum concentration (Cmax) of CSL312 in subjects with C1-INH HAE during Treatment Period 1

End point title	Maximum concentration (Cmax) of CSL312 in subjects with C1-INH HAE during Treatment Period 1[11]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[12]	9	8	7
Units: ug/mL				
arithmetic mean (standard deviation)	()	10.6 (± 6.09)	15.9 (± 5.22)	56.4 (± 15.9)

Notes:

[12] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	0[13]			
Units: ug/mL				
arithmetic mean (standard deviation)	()			

Notes:

[13] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the concentration-time curve in 1 dosing interval (AUC0-tau) of CSL312 in subjects with C1-INH HAE during Treatment Period 1

End point title	Area under the concentration-time curve in 1 dosing interval (AUC0-tau) of CSL312 in subjects with C1-INH HAE during Treatment Period 1[14]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[15]	9	8	7
Units: h*µg/mL				
arithmetic mean (standard deviation)	()	4507 (± 2424)	7166 (± 2410)	26514 (± 8151)

Notes:

[15] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	0[16]			
Units: h*µg/mL				
arithmetic mean (standard deviation)	()			

Notes:

[16] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

Statistical analyses

No statistical analyses for this end point

Secondary: Time of maximum concentration (Tmax) of CSL312 in subjects with C1-INH HAE during Treatment Period 1

End point title	Time of maximum concentration (Tmax) of CSL312 in subjects with C1-INH HAE during Treatment Period 1[17]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[18]	9	8	7
Units: hours				
median (full range (min-max))	(to)	143.38 (45.4 to 196)	165.51 (116 to 218)	165.63 (72.4 to 188)

Notes:

[18] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	0[19]			
Units: hours				
median (full range (min-max))	(to)			

Notes:

[19] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal elimination half-life (T1/2) of CSL312 in subjects with C1-INH HAE during Treatment Period 1

End point title	Terminal elimination half-life (T1/2) of CSL312 in subjects with C1-INH HAE during Treatment Period 1[20]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[21]	7	7	5
Units: hours				
arithmetic mean (standard deviation)	()	411.7 (± 96.97)	394.0 (± 85.64)	443.5 (± 44.00)

Notes:

[21] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	0[22]			
Units: hours				
arithmetic mean (standard deviation)	()			

Notes:

[22] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL/F) of CSL312 in subjects with C1-INH HAE during Treatment Period 1

End point title	Clearance (CL/F) of CSL312 in subjects with C1-INH HAE during Treatment Period 1[23]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[24]	9	8	7
Units: L/hour				
arithmetic mean (standard deviation)	()	0.0198 (± 0.0079)	0.0303 (± 0.0084)	0.0246 (± 0.0079)

Notes:

[24] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	0[25]			
Units: L/hour				
arithmetic mean (standard deviation)	()			

Notes:

[25] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of distribution during the elimination phase (Vz/F) of CSL312 in subjects with C1-INH HAE during Treatment Period 1

End point title	Volume of distribution during the elimination phase (Vz/F) of CSL312 in subjects with C1-INH HAE during Treatment Period 1[26]

End point description:

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[27]	7	7	5
Units: Liters				
arithmetic mean (standard deviation)	()	10.6 (± 5.10)	17.0 (± 4.78)	17.1 (± 6.67)

Notes:

[27] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	0[28]			
Units: Liters				
arithmetic mean (standard deviation)	()			

Notes:

[28] - The PK population consisted of all subjects with at least 1 measurable concentration of CSL312

Statistical analyses

No statistical analyses for this end point

Secondary: The number of subjects with C1-INH HAE with adverse events (AEs), serious adverse events (SAEs), adverse events of special interest (AESI), injection site reactions (ISRs), binding antibodies to CSL312 during Treatment Period 1

End point title	The number of subjects with C1-INH HAE with adverse events (AEs), serious adverse events (SAEs), adverse events of special interest (AESI), injection site reactions (ISRs), binding antibodies to CSL312 during Treatment Period 1[29]

End point description:

Adverse events of special interest is defined as anaphylaxis, thromboembolic events, and bleeding events.

End point type	Secondary

End point timeframe:

13 weeks

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CSL312 (FXII/PLG HAE) arm used for exploratory endpoints.

End point values	Placebo	CSL312 (low)	CSL312 (med)	CSL312 (high)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	7
Units: Number of participans				
number (not applicable)				
AEs	7	7	7	7
SAEs	0	0	0	0
AESI	1	0	0	0
ISRs	2	1	1	4
Binding Antibodies to CSL312	1	0	0	0

End point values	CSL312 (med/high)			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of participans				
number (not applicable)				
AEs	4			
SAEs	0			
AESI	0			
ISRs	2			
Binding Antibodies to CSL312	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 129 weeks per participant

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects with C1-INH HAE receiving buffer only.

Placebo: Buffer without active ingredient.

Reporting group title	CSL312 (low)

Reporting group description:

Subjects with C1-INH HAE receiving low dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (med)

Reporting group description:

Subjects with C1-INH HAE receiving medium dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (high)

Reporting group description:

Subjects with C1-INH HAE receiving high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (med/high)

Reporting group description:

Subjects with C1-INH HAE receiving medium/high dose CSL312.

Factor XIIa antagonist monoclonal antibody: Factor XIIa antagonist monoclonal antibody for intravenous and subcutaneous use.

Reporting group title	CSL312 (med-Period 2)

Reporting group description:

Subjects with C1-INH HAE receiving medium dose CSL312

Reporting group title	CSL312 (med/high-Period 2)

Reporting group description:

Subjects with C1-INH HAE receiving medium/high dose CSL312

Reporting group title	CSL312 (high-Period 2)

Reporting group description:

Subjects with C1-INH HAE receiving high dose CSL312

Reporting group title	CSL312 (FXII/PLG HAE-Period 1)

Reporting group description:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312

Reporting group title	CSL312 (FXII/PLG HAE-Period 2)

Reporting group description:

Subjects with FXII/PLG HAE (Hereditary Angioedema with Normal C1-esterase Inhibitor and Factor XII or Plasminogen Gene Mutation) receiving high dose CSL312

Serious adverse events	Placebo	CSL312 (low)	CSL312 (med)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (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 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (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
Gastrointestinal disorders			
Diverticular perforation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (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

Serious adverse events	CSL312 (high)	CSL312 (med/high)	CSL312 (med-Period 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
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 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (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

Gastrointestinal disorders			
Diverticular perforation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (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

Serious adverse events	CSL312 (med/high-Period 2)	CSL312 (high-Period 2)	CSL312 (FXII/PLG HAE-Period 1)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	1 / 6 (16.67%)
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 / 3 (0.00%)	0 / 18 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diverticular perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (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

Serious adverse events	CSL312 (FXII/PLG HAE-Period 2)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		

number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diverticular perforation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	CSL312 (low)	CSL312 (med)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	7 / 9 (77.78%)	7 / 8 (87.50%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Injection site erythema			
subjects affected / exposed	2 / 8 (25.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	2	0	1
Injection site pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injection site pruritus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	2
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Injection site swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injection site urticaria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Facial pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Throat tightness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspnoea at rest			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperventilation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Productive cough			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vascular access site bruising			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Ligament sprain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Limb injury			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

Vestibular disorder			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Photopsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 8 (25.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Urticaria			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Dermatitis			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Ingrowing nail			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Polymorphic light eruption			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Ureterolithiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Myalgia			

subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Plantar fascial fibromatosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bone swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	2 / 8 (25.00%)	2 / 9 (22.22%)	3 / 8 (37.50%)
occurrences (all)	2	2	3

Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Abscess limb			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nasal herpes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Hordeolum			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	CSL312 (high)	CSL312 (med/high)	CSL312 (med-Period 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)	4 / 6 (66.67%)	25 / 36 (69.44%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1

General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	2	0	1
Injection site pain			
subjects affected / exposed	3 / 7 (42.86%)	1 / 6 (16.67%)	0 / 36 (0.00%)
occurrences (all)	3	4	0
Chest discomfort			
subjects affected / exposed	2 / 7 (28.57%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Injection site pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Injection site swelling			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Injection site urticaria			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Facial pain			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Malaise			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Throat tightness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	2 / 36 (5.56%)
occurrences (all)	0	1	2
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Dyspnoea at rest			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hyperventilation			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Muscle strain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Vascular access site bruising			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	2
Limb injury			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 7 (28.57%)	2 / 6 (33.33%)	6 / 36 (16.67%)
occurrences (all)	3	5	12
Dizziness			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Nerve compression			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Anosmia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Lymphopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Photopsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	3
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	5 / 36 (13.89%)
occurrences (all)	0	0	7
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Inguinal hernia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Dental caries			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 7 (28.57%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0

Urticaria			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Dermatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Polymorphic light eruption			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Psoriasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ureterolithiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	3
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Plantar fascial fibromatosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	3 / 36 (8.33%)
occurrences (all)	0	1	3
Muscular weakness			
subjects affected / exposed	0 / 7 (0.00%)	1 / 6 (16.67%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Rotator cuff syndrome			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	4
Torticollis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Bone swelling			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	4 / 36 (11.11%)
occurrences (all)	0	0	4
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	3 / 36 (8.33%)
occurrences (all)	2	0	6
Abscess limb			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Nasal herpes			
subjects affected / exposed	1 / 7 (14.29%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	4
Sinusitis			

subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Cystitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 7 (0.00%)	0 / 6 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	CSL312 (med/high-Period 2)	CSL312 (high-Period 2)	CSL312 (FXII/PLG HAE-Period 1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	17 / 18 (94.44%)	1 / 6 (16.67%)
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypertension			

subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 3 (0.00%)	3 / 18 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Injection site pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	2 / 18 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Injection site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injection site swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Facial pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Throat tightness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	3 / 18 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dyspnoea at rest			

subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hyperventilation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	2 / 18 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vascular access site bruising			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 3 (0.00%)	4 / 18 (22.22%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nerve compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Anosmia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Photopsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	2 / 18 (11.11%)	1 / 6 (16.67%)
occurrences (all)	0	3	1
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 18 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dental caries			

subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Polymorphic light eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psoriasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Ureterolithiasis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 18 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Plantar fascial fibromatosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	4 / 18 (22.22%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Torticollis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Bone swelling			

subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 18 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Abscess limb			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Tonsillitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 18 (11.11%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Cystitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 18 (5.56%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 18 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	CSL312 (FXII/PLG HAE-Period 2)		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	2 / 2 (100.00%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Injection site pruritus			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Injection site swelling			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Injection site urticaria			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Facial pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Throat tightness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dyspnoea at rest			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Hyperventilation			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pulmonary congestion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Initial insomnia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Investigations			
SARS-CoV-2 test positive			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Muscle strain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Vascular access site bruising			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Skin laceration			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Nerve compression			

subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Anosmia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	 0 / 2 (0.00%) 0		
Ear and labyrinth disorders Vestibular disorder subjects affected / exposed occurrences (all)	 0 / 2 (0.00%) 0		
Eye disorders Photopsia subjects affected / exposed occurrences (all)	 0 / 2 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Dyspepsia	 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0		

subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Inguinal hernia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Ingrowing nail			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Polymorphic light eruption			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Psoriasis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Eczema			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Renal pain			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nephrolithiasis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Ureterolithiasis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 2 (50.00%)		
occurrences (all)	1		
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Plantar fascial fibromatosis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Rotator cuff syndrome			

subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Torticollis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Bone swelling			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Limb discomfort			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Abscess limb			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		
Nasal herpes			
subjects affected / exposed	0 / 2 (0.00%)		
occurrences (all)	0		

Oral herpes				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Urinary tract infection				
subjects affected / exposed	1 / 2 (50.00%)			
occurrences (all)	2			
Sinusitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Pneumonia				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Vulvovaginal mycotic infection				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
Bronchitis				
subjects affected / exposed	0 / 2 (0.00%)			
occurrences (all)	0			
COVID-19				
subjects affected / exposed	2 / 2 (100.00%)			
occurrences (all)	5			
Herpes zoster				
subjects affected / exposed	1 / 2 (50.00%)			
occurrences (all)	1			

Influenza subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2018	- Frequency of pregnancy testing was increased in Treatment Period 2. - Urine testing for pregnancy was added as an alternative to serum testing. - Acceptable methods of contraception were updated. - The requirement that pregnancy test results obtained outside of the study site would be documented and tracked was added. - The duration of the Follow-up Period was extended to 95 days. - Activities related to the accessibility and accountability of CSL312 were clarified, in the case that Treatment Period 2 was extended. - Acceptable use of routine (long-term) HAE prophylaxis during the study was clarified. - Clarification to the laboratory values that were to be documented in the medical history page of the eCRF. - Clarifications were made to statistical methods.
20 March 2020	- For subjects with C1-esterase inhibitor deficiency (C1-INH HAE) receiving the 600 mg dose in Treatment Period 2, the dose was decreased to 200 mg. - Edits were made to the Statistical Analysis and Methods section.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported