



Clinical trial results:

A multicenter, double-blind, randomized, placebo-controlled, parallel-arm study to investigate the efficacy and safety of subcutaneous administration of CSL312 (garadacimab) in the prophylactic treatment of hereditary angioedema

Summary

EudraCT number	2020-000570-25
Trial protocol	DE HU NL IT
Global end of trial date	07 June 2022

Results information

Result version number	v1 (current)
This version publication date	24 June 2023
First version publication date	24 June 2023

Trial information

Trial identification

Sponsor protocol code	CSL312_3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04656418
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring
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)	Yes
EMA paediatric investigation plan number(s)	EMA-002726-PIP01-19
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	07 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of subcutaneous (SC) administration of CSL312 (garadacimab) in the prophylactic treatment of hereditary angioedema.

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	27 January 2021
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	Netherlands: 3
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	United States: 21
Country: Number of subjects enrolled	Japan: 6
Worldwide total number of subjects	64
EEA total number of subjects	20

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)	6
Adults (18-64 years)	52
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at study centers in Canada, Germany, Hungary, Israel, Japan, Netherlands, and the United States from 27 January 2021 to 07 June 2022.

Pre-assignment

Screening details:

A total of 80 subjects were screened, of which 64 subjects were randomised and received the loading dose in the treatment period.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	CSL312

Arm description:

Subjects received a CSL312 loading dose of 400 mg as two 200 mg SC injections in Month 1 along with CSL312 of 200 mg SC injections, once monthly from Months 2 to 6.

Arm type	Experimental
Investigational medicinal product name	CSL312
Investigational medicinal product code	
Other name	Factor XIIa inhibitor monoclonal antibody, garadacimab
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A loading dose of 400 mg as two 200 mg injections in Month 1 along with 200 mg injections, once monthly from Months 2 to 6.

Arm title	Placebo
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Arm description:

Subjects received a CSL312 matched loading dose of placebo as two SC injections in Month 1 along with CSL312 matched placebo SC injections, once monthly from Months 2 to 6.

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

Dosage and administration details:

A CSL312 matched loading dose of placebo as two injections in Month 1 along with CSL312 matched placebo injections, once monthly from Months 2 to 6.

Number of subjects in period 1	CSL312	Placebo
Started	39	25
Completed	38	22
Not completed	1	3
Withdrawal by subject	1	3

Baseline characteristics

Reporting groups

Reporting group title	CSL312
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Reporting group description:

Subjects received a CSL312 loading dose of 400 mg as two 200 mg SC injections in Month 1 along with CSL312 of 200 mg SC injections, once monthly from Months 2 to 6.

Reporting group title	Placebo
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Reporting group description:

Subjects received a CSL312 matched loading dose of placebo as two SC injections in Month 1 along with CSL312 matched placebo SC injections, once monthly from Months 2 to 6.

Reporting group values	CSL312	Placebo	Total
Number of subjects	39	25	64
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	43.3 ± 17.45	37.8 ± 12.80	-
Gender categorical Units: Subjects			
Female	24	14	38
Male	15	11	26
Ethnicity Units: Subjects			
Hispanic or Latino	1	2	3
Not Hispanic or Latino	37	23	60
Unknown or Not Reported	1	0	1
Race Units: Subjects			
Asian	4	2	6
Black or African American	0	1	1
Native Hawaiian or Other Pacific Islander	1	0	1
White	33	22	55
Other	1	0	1

End points

End points reporting groups

Reporting group title	CSL312
Reporting group description: Subjects received a CSL312 loading dose of 400 mg as two 200 mg SC injections in Month 1 along with CSL312 of 200 mg SC injections, once monthly from Months 2 to 6.	
Reporting group title	Placebo
Reporting group description: Subjects received a CSL312 matched loading dose of placebo as two SC injections in Month 1 along with CSL312 matched placebo SC injections, once monthly from Months 2 to 6.	
Subject analysis set title	CSL312 and Placebo Comparison Group
Subject analysis set type	Intention-to-treat
Subject analysis set description: CSL312: Subjects received a CSL312 loading dose of 400 mg as two 200 mg SC injections in Month 1 along with CSL312 of 200 mg SC injections, once monthly from Months 2 to 6. Placebo: Subjects received a CSL312 matched loading dose of placebo as two SC injections in Month 1 along with CSL312 matched placebo SC injections, once monthly from Months 2 to 6.	

Primary: Time-Normalised Number of Hereditary Angioedema (HAE) Attacks per Month During Treatment Period

End point title	Time-Normalised Number of Hereditary Angioedema (HAE) Attacks per Month During Treatment Period
End point description: Time-normalised number of HAE attacks per month during treatment was calculated per subject as: [number of HAE attacks / length of subject treatment in days] * 30.4375. ITT analysis set included all the randomised subjects who provided written informed consent and underwent study screening procedures. 'Number of subjects analysed' indicates the number of subjects with data available for endpoint analysis.	
End point type	Primary
End point timeframe: First injection up to 6 months	

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	24		
Units: number of HAE attacks per month				
arithmetic mean (standard deviation)	0.27 (± 0.683)	2.01 (± 1.341)		

Statistical analyses

Statistical analysis title	CSL312 vs Placebo
Comparison groups	CSL312 v Placebo

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	< 0.001 ^[2]
Method	Two-sided Wilcoxon test

Notes:

[1] - Test for differences

[2] - Compared the time-normalised number of HAE attacks in the active and placebo arms by using a two-sided Wilcoxon test (Hierarchical Testing H01) at alpha = 5%.

Secondary: Percentage Change in the Time-Normalised Number of HAE Attacks per Month During the Treatment Period Compared to the Run-in Period

End point title	Percentage Change in the Time-Normalised Number of HAE Attacks per Month During the Treatment Period Compared to the Run-in Period
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End point description:

Percentage change in the time-normalised number of HAE attacks was calculated within a subject as: $100 * [1 - (\text{time-normalised number of HAE attacks per month during treatment period} / \text{time-normalised number of HAE attacks per month during run-in period})]$. Time-normalised number of HAE attacks per month during treatment period was calculated per subject as: $[\text{number of HAE attacks} / \text{length of subject treatment in days}] * 30.4375$. ITT analysis set included all the randomised subjects who provided written informed consent and underwent study screening procedures. 'Number of subjects analysed' indicates the number of subjects with data available for endpoint analysis. 'Number analysed (n)' indicates the number of subjects with data available for analysis at the specified time point.

End point type	Secondary
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End point timeframe:

6 months, first 3-months and second 3-months of treatment period

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	24		
Units: percentage change in HAE attacks/month				
arithmetic mean (standard deviation)				
6 Months of Treatment (n=39, 24)	90.67 (± 22.433)	20.21 (± 42.661)		
First 3-months of Treatment (n=39, 24)	91.10 (± 21.255)	18.89 (± 53.837)		
Second 3-months of Treatment (n=39, 22)	90.12 (± 25.624)	29.87 (± 55.529)		

Statistical analyses

Statistical analysis title	CSL312 vs Placebo
Statistical analysis description:	
6 Months of treatment	
Comparison groups	CSL312 v Placebo

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	< 0.001 ^[4]
Method	Two-sided Wilcoxon test

Notes:

[3] - Test for differences

[4] - Compared the time-normalised number of HAE attacks in the active and placebo arms by using a two-sided Wilcoxon test.

Secondary: Time-Normalised Number of HAE Attacks per Month Requiring On-Demand Treatment

End point title	Time-Normalised Number of HAE Attacks per Month Requiring On-Demand Treatment
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End point description:

Time-normalised number of HAE attacks per month requiring on-demand treatment was calculated per subjects as: [number of HAE attacks requiring on-demand treatment / length of subject treatment in days] * 30.4375. ITT analysis set included all the randomised subjects who provided written informed consent and underwent study screening procedures. 'Number of subjects analysed' indicates the number of subjects with data available for endpoint analysis. 'Number analysed (n)' indicates the total number of HAE attacks available for analysis at the specified time point.

End point type	Secondary
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End point timeframe:

6 months, first 3-months and second 3-months of treatment period

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39 ^[5]	24 ^[6]		
Units: number of HAE attacks per month				
arithmetic mean (standard deviation)				
6 Months of Treatment (n=63, 264)	0.23 (± 0.663)	1.86 (± 1.412)		
First 3-months of Treatment (n=31, 144)	0.24 (± 0.748)	1.76 (± 1.378)		
Second 3-months of Treatment (n=32, 120)	0.23 (± 0.610)	1.80 (± 1.626)		

Notes:

[5] - Overall units analysed: 63 total number of HAE attacks

[6] - Overall units analysed: 264 total number of HAE attacks; 22 subjects for Second 3-months of treatment

Statistical analyses

Statistical analysis title	CSL312 vs Placebo
Statistical analysis description:	
6 Months of treatment	
Comparison groups	CSL312 v Placebo

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[7]
P-value	< 0.001 ^[8]
Method	Two-sided Wilcoxon test

Notes:

[7] - Test for differences

[8] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at alpha = 5%.

Statistical analysis title	CSL312 vs Placebo
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Statistical analysis description:

First 3-months of treatment

Comparison groups	CSL312 v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[9]
P-value	< 0.001 ^[10]
Method	Two-sided Wilcoxon test

Notes:

[9] - Test for differences

[10] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at alpha = 5%.

Statistical analysis title	CSL312 vs Placebo
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Statistical analysis description:

Second 3-months of treatment

Comparison groups	CSL312 v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[11]
P-value	< 0.001 ^[12]
Method	Two-sided Wilcoxon test

Notes:

[11] - Test for differences

[12] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at alpha = 5%.

Secondary: Time-Normalised Number of Moderate or Severe HAE Attacks per Month

End point title	Time-Normalised Number of Moderate or Severe HAE Attacks per Month
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End point description:

Time-normalised number of moderate or severe HAE attacks per month during treatment period was calculated per subject as: [number of moderate or severe HAE attacks / length of subject treatment in days] * 30.4375. ITT analysis set included all the randomised subjects who provided written informed consent and underwent study screening procedures. 'Number of subjects analysed' indicates the number of subjects with data available for endpoint analysis. 'Number analysed (n)' indicates the number of subjects with data available for analysis at the specified time point.

End point type	Secondary
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End point timeframe:

6 months, first 3-months and second 3-months of treatment period

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39 ^[13]	24 ^[14]		
Units: number of HAE attacks per month				
arithmetic mean (standard deviation)				
6 Months of Treatment (n=39, 24)	0.13 (± 0.296)	1.35 (± 1.166)		
First 3-months of Treatment (n=39,24)	0.12 (± 0.305)	1.25 (± 1.091)		
Second 3-months of Treatment (n=39,22)	0.13 (± 0.320)	1.24 (± 1.296)		

Notes:

[13] - Overall Number of Units Analysed: 63 total number of HAE attacks

[14] - Overall Number of Units Analysed: 264 total number of HAE attacks

Statistical analyses

Statistical analysis title	CSL312 vs Placebo
Statistical analysis description:	
6 Months of treatment	
Comparison groups	CSL312 v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[15]
P-value	< 0.001 ^[16]
Method	Two-sided Wilcoxon test

Notes:

[15] - Test for differences

[16] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at alpha = 5%.

Statistical analysis title	CSL312 vs Placebo
Statistical analysis description:	
First 3-months of treatment	
Comparison groups	CSL312 v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[17]
P-value	< 0.001 ^[18]
Method	Two-sided Wilcoxon test

Notes:

[17] - Test for differences

[18] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at alpha = 5%.

Statistical analysis title	CSL312 vs Placebo
Statistical analysis description:	
Second 3-months of treatment	
Comparison groups	CSL312 v Placebo

Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[19]
P-value	< 0.001 ^[20]
Method	Two-sided Wilcoxon test

Notes:

[19] - Test for differences

[20] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at alpha = 5%

Secondary: Time-Normalised Number of HAE Attacks per Month in the First 3-months and Second 3-months of Treatment Period

End point title	Time-Normalised Number of HAE Attacks per Month in the First 3-months and Second 3-months of Treatment Period
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End point description:

Time-normalised number of HAE attacks per month during treatment was calculated per subject as: [number of HAE attacks / length of subject treatment in days] * 30.4375. ITT analysis set included all the randomised subjects who provided written informed consent and underwent study screening procedures. 'Number of subjects analysed' indicates the number of subjects with data available for endpoint analysis. 'Number analysed (n)' indicates the number of subjects with data available for analysis at the specified time point.

End point type	Secondary
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End point timeframe:

First 3-months and second 3-months of treatment period

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	24		
Units: number of HAE attacks per month				
arithmetic mean (standard deviation)				
First 3-months of Treatment (n=39, 24)	0.26 (± 0.749)	1.97 (± 1.287)		
Second 3-months of Treatment (n=39, 22)	0.28 (± 0.652)	1.86 (± 1.603)		

Statistical analyses

Statistical analysis title	CSL312 vs Placebo
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Statistical analysis description:

First 3-months of treatment

Comparison groups	CSL312 v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[21]
P-value	< 0.001 ^[22]
Method	Two-sided Wilcoxon test

Notes:

[21] - Test for differences

[22] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at

alpha = 5%.

Statistical analysis title	CSL312 vs Placebo
Statistical analysis description: Second 3-months of treatment	
Comparison groups	CSL312 v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	other ^[23]
P-value	< 0.001 ^[24]
Method	Two-sided Wilcoxon test

Notes:

[23] - Test for differences

[24] - Tested the differences between the active and placebo arms using a two-sided Wilcoxon test at alpha = 5%.

Secondary: Relative Difference in Means in the Time-Normalised Number of HAE Attacks per Month Between CSL312 to Placebo

End point title	Relative Difference in Means in the Time-Normalised Number of HAE Attacks per Month Between CSL312 to Placebo
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End point description:

Relative difference in means in time-normalised number of HAE attacks/month CSL312 to Placebo was calculated as: $100 * [(\text{mean time-normalised number of HAE attacks for CSL312} - \text{mean time-normalised number of HAE attacks for placebo}) / \text{mean time-normalised number of HAE attacks for placebo}]$. Time-normalised number of HAE attacks/month during treatment was calculated per subject as: $[\text{number of HAE attacks} / \text{subject treatment length(days)}] * 30.4375$. ITT analysis set included all the randomised subjects who provided written informed consent and underwent study screening procedures. 'Number of subjects analysed' = number of subjects with data available for endpoint analysis. 'n' = number of subjects with data available for analysis at specified time point. As pre-specified in protocol and SAP, data was reported for subjects between CSL312 and Placebo comparison group.

End point type	Secondary
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End point timeframe:

6 months, first 3-months and second 3-months of treatment period

End point values	CSL312 and Placebo Comparison Group			
Subject group type	Subject analysis set			
Number of subjects analysed	63			
Units: number of HAE attacks per month				
arithmetic mean (confidence interval 95%)				
6 Months of Treatment	-86.51 (-95.68 to -57.84)			
First 3-months of Treatment	-86.64 (-95.87 to -56.76)			
Second 3-months of Treatment (n=61)	-85.01 (-95.62 to -48.74)			

Attachments (see zip file)	Relative Difference in Means in the Time-Normalise/Time-
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Response to Subject's Global Assessment of Response to Therapy (SGART)

End point title	Percentage of Subjects With a Response to Subject's Global Assessment of Response to Therapy (SGART)
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End point description:

SGART is a self-assessment by the subject and measures the subject's overall treatment response to the investigational product using the following ratings: 0 (none: worse or no response at all, not acceptable), 1 (poor: very little response, not acceptable), 2 (fair: some response, acceptable but could be better), 3 (good: good response, acceptable), and 4 (excellent: excellent response, as good as can be imagined). ITT analysis set included all the randomised subjects who provided written informed consent and underwent study screening procedures. 'Number of subjects analysed' indicates the number of subjects with data available for endpoint analysis.

End point type	Secondary
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End point timeframe:

Up to 6 months

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	24		
Units: percentage of subjects				
number (not applicable)				
None	2.6	41.7		
Poor	7.9	16.7		
Fair	7.9	8.3		
Good	15.8	20.8		
Excellent	65.8	12.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With at Least One Adverse Event (AE), Serious Adverse Event (SAE), and AEs of Special Interest (AESI)

End point title	Number of Subjects With at Least One Adverse Event (AE), Serious Adverse Event (SAE), and AEs of Special Interest (AESI)
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End point description:

AE is any untoward medical occurrence in a subject administered with an investigational product which does not necessarily have a causal relationship with treatment, can be any unfavorable and unintended sign, symptom, or disease temporally associated with use of an investigational product, whether or not considered related to product. SAE is any untoward medical occurrence that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, is a congenital anomaly or birth defect, or is a medically significant event. An AESI is an AE of scientific and medical concern specific to sponsor's product or program, for which ongoing monitoring and rapid communication by investigator to sponsor is appropriate. Safety analysis set included all the randomised

subjects who provided written informed consent, underwent study screening procedures and received at least 1 dose of the investigational product.

End point type	Secondary
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End point timeframe:

From first dose of study drug up to 3 months after the last injection (approximately 8 months)

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	25		
Units: subjects				
AE	25	15		
SAE	1	0		
AESI	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With CSL312-induced Anti-CSL312 Antibodies

End point title	Number of Subjects With CSL312-induced Anti-CSL312 Antibodies
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End point description:

Safety analysis set included all the randomised subjects who provided written informed consent, underwent study screening procedures and received at least 1 dose of the investigational product.

End point type	Secondary
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End point timeframe:

Up to 8 months

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	25		
Units: subjects	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Laboratory Assessments Reported as Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Clinically Significant Abnormalities in Laboratory Assessments Reported as Treatment Emergent Adverse Events (TEAEs)
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End point description:

Laboratory assessments included: Hematology, biochemistry, urinalysis, and coagulation parameters. Safety analysis set included all the randomised subjects who provided written informed consent, underwent study screening procedures and received at least 1 dose of the investigational product.

End point type	Secondary
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End point timeframe:

From first dose of study drug up to 3 months after the last injection (approximately 8 months)

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	25		
Units: subjects	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least One AE, SAE, and AESI

End point title	Percentage of Subjects With at Least One AE, SAE, and AESI
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End point description:

AE is any untoward medical occurrence in a subject administered with an investigational product which does not necessarily have a causal relationship with treatment, can be any unfavorable and unintended sign, symptom, or disease temporally associated with use of an investigational product, whether or not considered related to product. SAE is any untoward medical occurrence that results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, is a congenital anomaly or birth defect, or is a medically significant event. An AESI is an AE of scientific and medical concern specific to sponsor's product or program, for which ongoing monitoring and rapid communication by investigator to sponsor is appropriate. Safety analysis set included all the randomised subjects who provided written informed consent, underwent study screening procedures and received at least 1 dose of the investigational product.

End point type	Secondary
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End point timeframe:

From first dose of study drug up to 3 months after the last injection (approximately 8 months)

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	25		
Units: percentage of subjects				
number (not applicable)				
AE	64.1	60.0		
SAE	2.6	0		
AESI	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With CSL312-induced Anti-CSL312 Antibodies

End point title	Percentage of Subjects With CSL312-induced Anti-CSL312 Antibodies
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End point description:

Safety analysis set included all the randomised subjects who provided written informed consent, underwent study screening procedures and received at least 1 dose of the investigational product.

End point type	Secondary
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End point timeframe:

Up to 6 months

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	25		
Units: percentage of subjects				
number (not applicable)	2.6	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinically Significant Abnormalities in Laboratory Assessments Reported as TEAEs

End point title	Percentage of Subjects With Clinically Significant Abnormalities in Laboratory Assessments Reported as TEAEs
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End point description:

Laboratory assessments included: Hematology, biochemistry, urinalysis, and coagulation parameters. Safety analysis set included all the randomised subjects who provided written informed consent, underwent study screening procedures and received at least 1 dose of the investigational product.

End point type	Secondary
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End point timeframe:

From first dose of study drug up to 3 months after the last injection (approximately 8 months)

End point values	CSL312	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	25		
Units: percentage of subjects				
number (not applicable)	2.6	8.0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to 3 months after the last injection (approximately 8 months)

Adverse event reporting additional description:

Safety analysis set included all the randomised subjects who provided written informed consent, underwent study screening procedures and received at least 1 dose of the investigational product.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	CSL312
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Reporting group description:

Subjects received a CSL312 loading dose of 400 mg as two 200 mg SC injections in Month 1 along with CSL312 of 200 mg SC injections, once monthly from Months 2 to 6.

Reporting group title	Placebo
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Reporting group description:

Subjects received a CSL312 matched loading dose of placebo as two SC injections in Month 1 along with CSL312 matched placebo SC injections, once monthly from Months 2 to 6.

Serious adverse events	CSL312	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 39 (2.56%)	0 / 25 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Hereditary angioedema			
subjects affected / exposed	1 / 39 (2.56%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CSL312	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 39 (43.59%)	12 / 25 (48.00%)	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 9	4 / 25 (16.00%) 4	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Injection site erythema subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0 1 / 39 (2.56%) 1 1 / 39 (2.56%) 1	3 / 25 (12.00%) 5 2 / 25 (8.00%) 2 2 / 25 (8.00%) 2	
Eye disorders Visual impairment subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 25 (0.00%) 0	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2 2 / 39 (5.13%) 2 0 / 39 (0.00%) 0	1 / 25 (4.00%) 1 0 / 25 (0.00%) 0 2 / 25 (8.00%) 2	
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	1 / 25 (4.00%) 1	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Pain in extremity	2 / 39 (5.13%) 2 2	1 / 25 (4.00%) 1 1	

subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 25 (8.00%) 3	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 39 (10.26%)	2 / 25 (8.00%)	
occurrences (all)	4	2	
Nasopharyngitis			
subjects affected / exposed	3 / 39 (7.69%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
COVID-19			
subjects affected / exposed	0 / 39 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Gastrointestinal infection			
subjects affected / exposed	2 / 39 (5.13%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Conjunctivitis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Sinusitis			
subjects affected / exposed	2 / 39 (5.13%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Urinary tract infection			
subjects affected / exposed	2 / 39 (5.13%)	0 / 25 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported