



## 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     |
| <b>Arm title</b>             | 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | 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.

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | 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.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | 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

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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.

|  |                        |
|--|------------------------|
| <b>Arm title</b>   | CSL312 (high)          |
| Arm description:<br>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.

|   |                        |
|---|------------------------|
| <b>Arm title</b>  | CSL312 (FXII/PLG HAE)  |
| Arm description:<br>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.

| <b>Number of subjects in period 2<sup>[1]</sup></b> | 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:<br>Subjects with C1-INH HAE receiving buffer only.   |                       |
| Placebo: Buffer without active ingredient.  |                       |
| Reporting group title   | CSL312 (low)          |
| Reporting group description:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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 <sup>[1]</sup> |
|-----------------|---|

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) |

|   |                              |
|---|------------------------------|
| <b>Statistical analysis title</b>       | 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 <sup>[2]</sup> |
|-----------------|---|

End point description:

Response is defined as a  $\geq 50\%$  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 <sup>[3]</sup> |
|-----------------|---|

End point description:

Response is defined as a  $\geq 50\%$  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 <sup>[4]</sup> |
|-----------------|---|

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 <sup>[5]</sup> |
|-----------------|---|

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 <sup>[6]</sup> |
|-----------------|---|

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<sup>[7]</sup>

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<sup>[8]</sup>

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 <sup>[9]</sup> |
|-----------------|---|

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 <sup>[10]</sup> |
|-----------------|--|

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 <sup>[11]</sup> |
|-----------------|--|

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 <sup>[12]</sup> | 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 <sup>[13]</sup> |  |  |  |
| 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 <sup>[14]</sup> |
|-----------------|---|

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 <sup>[15]</sup> | 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 <sup>[16]</sup> |  |  |  |
| 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 <sup>[17]</sup> |
|-----------------|--|

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 <sup>[18]</sup> | 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 <sup>[19]</sup> |  |  |  |
| 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 <sup>[20]</sup> |
|-----------------|---|

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 <sup>[21]</sup> | 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 <sup>[22]</sup> |  |  |  |
| 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 <sup>[23]</sup> |
|-----------------|--|

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 <sup>[24]</sup> | 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 <sup>[25]</sup> |  |  |  |
| 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 (V<sub>z</sub>/F) of CSL312 in subjects with C1-INH HAE during Treatment Period 1

|                 |   |
|-----------------|---|
| End point title | Volume of distribution during the elimination phase (V <sub>z</sub> /F) of CSL312 in subjects with C1-INH HAE during Treatment Period 1 <sup>[26]</sup> |
|-----------------|---|

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 <sup>[27]</sup> | 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 <sup>[28]</sup> |  |  |  |
| 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 <sup>[29]</sup> |
|-----------------|---|

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.

| <b>End point values</b>       | 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)       |                 |                 |                 |                 |
| 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               |

| <b>End point values</b>       | CSL312 (med/high) |  |  |  |
|-------------------------------|-------------------|--|--|--|
| Subject group type            | Reporting group   |  |  |  |
| Number of subjects analysed   | 6                 |  |  |  |
| Units: Number of participants |                   |  |  |  |
| 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) |
|-----------------------|--------------------------------|



| <b>Serious adverse events</b>                     | 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         |

| <b>Serious adverse events</b>                     | 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          |

| <b>Serious adverse events</b>                     | 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                          |

| <b>Serious adverse events</b>                     | 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 %

| <b>Non-serious adverse events</b>                     | 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<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Malaise<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Immune system disorders<br>Food allergy<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Social circumstances<br>Pregnancy of partner<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 1 / 8 (12.50%)<br>1 |
| Throat tightness<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Cough<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Dyspnoea at rest<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |
| Hyperventilation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |

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

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

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

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

|   |                     |                    |                     |
|---|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Productive cough<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Pulmonary congestion<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Psychiatric disorders<br>Initial insomnia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 7 (14.29%)<br>1 | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Investigations<br>SARS-CoV-2 test positive<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 1 / 36 (2.78%)<br>1 |
| Glycosylated haemoglobin increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0 |
| Injury, poisoning and procedural complications<br>Contusion<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 2 / 36 (5.56%)<br>3 |
| Muscle strain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>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<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0  |
| Ear and labyrinth disorders<br>Vestibular disorder<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0  |
| Eye disorders<br>Photopsia<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Nausea<br>subjects affected / exposed<br>occurrences (all)               | 1 / 7 (14.29%)<br>1 | 0 / 6 (0.00%)<br>0 | 1 / 36 (2.78%)<br>3  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 5 / 36 (13.89%)<br>7 |
| Gastroesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0  |
| Toothache<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 2 / 36 (5.56%)<br>2  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 2 / 36 (5.56%)<br>2  |
| Inguinal hernia<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 2 / 36 (5.56%)<br>2  |
| Dental caries<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 7 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Rash<br>subjects affected / exposed<br>occurrences (all)     | 2 / 7 (28.57%)<br>2 | 0 / 6 (0.00%)<br>0 | 0 / 36 (0.00%)<br>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              |

| <b>Non-serious adverse events</b>                     | 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<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Pregnancy, puerperium and perinatal conditions<br>Pregnancy<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 3 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| General disorders and administration site conditions<br>Injection site erythema<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 3 / 18 (16.67%)<br>6 | 0 / 6 (0.00%)<br>0  |
| Injection site pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 1 / 18 (5.56%)<br>2  | 0 / 6 (0.00%)<br>0  |
| Chest discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 1 / 18 (5.56%)<br>2  | 0 / 6 (0.00%)<br>0  |
| Injection site pruritus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 2 / 18 (11.11%)<br>4 | 0 / 6 (0.00%)<br>0  |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Injection site urticaria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>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<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 1 / 18 (5.56%)<br>3  | 0 / 6 (0.00%)<br>0  |
| Anosmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Blood and lymphatic system disorders<br>Lymphopenia<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Ear and labyrinth disorders<br>Vestibular disorder<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Eye disorders<br>Photopsia<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 3 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Nausea<br>subjects affected / exposed<br>occurrences (all)                | 0 / 3 (0.00%)<br>0  | 2 / 18 (11.11%)<br>3 | 1 / 6 (16.67%)<br>1 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 3 (33.33%)<br>1 | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Toothache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 2 / 18 (11.11%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Inguinal hernia<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 3 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Dental caries   |                     |                      |                     |

|  |                    |                     |                    |
|--|--------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 6 (0.00%)<br>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             |

|   |                                   |  |  |
|---|-----------------------------------|--|--|
| <b>Non-serious adverse events</b>                     | CSL312 (FXII/PLG<br>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                              |                |  |  |

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

|  |                |  |  |
|--|----------------|--|--|
| 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             |  |  |
| <b>Torticollis</b>                       |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Bone swelling</b>                     |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Intervertebral disc protrusion</b>    |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Limb discomfort</b>                   |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Infections and infestations</b>       |               |  |  |
| <b>Upper respiratory tract infection</b> |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Nasopharyngitis</b>                   |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Abscess limb</b>                      |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Cellulitis</b>                        |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Gastroenteritis</b>                   |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Gingivitis</b>                        |               |  |  |
| subjects affected / exposed              | 0 / 2 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| <b>Nasal herpes</b>                      |               |  |  |
| 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<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 |  |  |
|---|---------------------|--|--|



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 18 December 2018 | <ul style="list-style-type: none"><li>- Frequency of pregnancy testing was increased in Treatment Period 2.</li><li>- Urine testing for pregnancy was added as an alternative to serum testing.</li><li>- Acceptable methods of contraception were updated.</li><li>- The requirement that pregnancy test results obtained outside of the study site would be documented and tracked was added.</li><li>- The duration of the Follow-up Period was extended to 95 days.</li><li>- Activities related to the accessibility and accountability of CSL312 were clarified, in the case that Treatment Period 2 was extended.</li><li>- Acceptable use of routine (long-term) HAE prophylaxis during the study was clarified.</li><li>- Clarification to the laboratory values that were to be documented in the medical history page of the eCRF.</li><li>- Clarifications were made to statistical methods.</li></ul> |
| 20 March 2020    | <ul style="list-style-type: none"><li>- 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.</li><li>- Edits were made to the Statistical Analysis and Methods section.</li></ul>  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported