



## Clinical trial results:

**A multi-center, double-blinded and open-label extension study to evaluate the efficacy and safety of ligelizumab as retreatment, self-administered therapy and monotherapy in Chronic Spontaneous Urticaria patients who completed studies CQGE031C2302, CQGE031C2303, CQGE031C2202 or CQGE031C1301**

### Summary

|                          |  |
|--------------------------|--|
| EudraCT number           | 2019-001792-37                                     |
| Trial protocol           | HU FR CZ ES DE AT GR EE IT BE SK DK PL NL BG HR RO |
| Global end of trial date | 01 September 2022                                  |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v2 (current)   |
| This version publication date  | 02 August 2023 |
| First version publication date | 03 March 2023  |
| Version creation reason        |                |

### Trial information

#### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | CQGE031C2302E1 |
|-----------------------|----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04210843 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharma AG  |
| Sponsor organisation address | CH-4002, Basel, Switzerland,  |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com |

Notes:

### Paediatric regulatory details

|  |     |
|--|-----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No  |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 01 September 2022 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 01 September 2022 |
| Was the trial ended prematurely?                     | Yes               |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the efficacy of ligelizumab assessed as the proportion of subjects achieving weekly urticaria activity score (UAS7)  $\leq 6$  after 12 weeks of retreatment, in subjects previously treated in CQGE031C2302/CQGE031C2303 (the core studies) as well as in the subset of subjects who previously achieved UAS7  $\leq 6$  in the core studies.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy:

This study required concurrent use of one second-generation H1-AH at local label-approved doses as background medication except for the subgroup of subjects who were offered a choice to go off background medication in the second half of the treatment period.

The investigator instructed the subject to notify the study site about any new medications he/she takes after the subject was enrolled into the study. Each concomitant drug was individually assessed against all exclusion criteria/prohibited medication and was captured in the study eCRF.

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 08 April 2020 |
| 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 | Argentina: 81 |
| Country: Number of subjects enrolled | Australia: 5  |
| Country: Number of subjects enrolled | Austria: 2    |
| Country: Number of subjects enrolled | Belgium: 1    |
| Country: Number of subjects enrolled | Brazil: 39    |
| Country: Number of subjects enrolled | Bulgaria: 17  |
| Country: Number of subjects enrolled | Canada: 24    |
| Country: Number of subjects enrolled | Chile: 19     |
| Country: Number of subjects enrolled | Colombia: 4   |
| Country: Number of subjects enrolled | Croatia: 4    |
| Country: Number of subjects enrolled | Czechia: 15   |
| Country: Number of subjects enrolled | Denmark: 7    |
| Country: Number of subjects enrolled | Estonia: 5    |

|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | France: 18              |
| Country: Number of subjects enrolled | Germany: 92             |
| Country: Number of subjects enrolled | United Kingdom: 1       |
| Country: Number of subjects enrolled | Greece: 13              |
| Country: Number of subjects enrolled | Guatemala: 5            |
| Country: Number of subjects enrolled | Hungary: 6              |
| Country: Number of subjects enrolled | India: 48               |
| Country: Number of subjects enrolled | Israel: 11              |
| Country: Number of subjects enrolled | Italy: 3                |
| Country: Number of subjects enrolled | Japan: 67               |
| Country: Number of subjects enrolled | Korea, Republic of: 49  |
| Country: Number of subjects enrolled | Lebanon: 13             |
| Country: Number of subjects enrolled | Malaysia: 14            |
| Country: Number of subjects enrolled | Mexico: 13              |
| Country: Number of subjects enrolled | Netherlands: 11         |
| Country: Number of subjects enrolled | Oman: 6                 |
| Country: Number of subjects enrolled | Peru: 7                 |
| Country: Number of subjects enrolled | Philippines: 4          |
| Country: Number of subjects enrolled | Poland: 50              |
| Country: Number of subjects enrolled | Romania: 9              |
| Country: Number of subjects enrolled | Russian Federation: 120 |
| Country: Number of subjects enrolled | Singapore: 3            |
| Country: Number of subjects enrolled | Slovakia: 14            |
| Country: Number of subjects enrolled | South Africa: 18        |
| Country: Number of subjects enrolled | Spain: 24               |
| Country: Number of subjects enrolled | Taiwan: 30              |
| Country: Number of subjects enrolled | Thailand: 23            |
| Country: Number of subjects enrolled | Tunisia: 16             |
| Country: Number of subjects enrolled | Turkey: 19              |
| Country: Number of subjects enrolled | United States: 95       |
| Country: Number of subjects enrolled | Viet Nam: 8             |
| Worldwide total number of subjects   | 1033                    |
| EEA total number of subjects         | 291                     |

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)                 | 40  |
| Adults (18-64 years)                      | 929 |
| From 65 to 84 years                       | 64  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 1457 participants who completed preceding studies (CQGE031C2302, CQGE031C2303, CQGE031C2202 or CQGE031C1301) entered the screening period. 515 participants with UAS7 <16 during screening entered the OBS1 period. A total of 1033 participants with UAS7 ≥ 16 during screening or OBS1 period were assigned to 1 of the 2 treatment arms.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | First half treatment period (52 weeks) |
| Is this the baseline period? | Yes                                    |
| Allocation method            | Non-randomised - controlled            |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer           |

Blinding implementation details:

Participants transitioning from CQGE031C2302 and CQGE031C2303 were treated in a double-blind manner for the first 12 weeks of treatment. Thereafter, they were treated in an open-label manner. No blinding was required for participants transitioning from CQGE031C1301 and CQGE031C2202

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS |

Arm description:

Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Ligelizumab                                  |
| Investigational medicinal product code | CQGE031                                      |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Ligelizumab            |
| Investigational medicinal product code | CQGE031                |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Ligelizumab 72 mg liquid in vial (LIVI) subcutaneously (s.c.) every 4 weeks (Q4W)

|                  |   |
|------------------|---|
| <b>Arm title</b> | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS |
|------------------|---|

Arm description:

Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |  |
|--|--|
| Investigational medicinal product name | Ligelizumab                                  |
| Investigational medicinal product code | CQGE031                                      |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Ligelizumab            |
| Investigational medicinal product code | CQGE031                |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Ligelizumab 120 mg liquid in vial (LIVI) subcutaneously (s.c.) every 4 weeks (Q4W)

| <b>Number of subjects in period 1</b> | Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS |
|---------------------------------------|--|---|
| Started                               | 290  | 743   |
| Completed                             | 140  | 369   |
| Not completed                         | 150  | 374   |
| Adverse event, serious fatal          | -  | 2   |
| Physician decision                    | -  | 3   |
| Subject decision                      | 11   | 28  |
| Adverse event, non-fatal              | 1  | 11  |
| Protocol deviation                    | -  | 3   |
| Pregnancy                             | -  | 1   |
| Study terminated by sponsor           | 134  | 322   |
| Lost to follow-up                     | 4  | 2   |
| Lack of efficacy                      | -  | 2   |

## Period 2

|                              |   |
|------------------------------|---|
| Period 2 title               | Second half treatment period (52 weeks) |
| Is this the baseline period? | No                                      |
| Allocation method            | Non-randomised - controlled             |
| Blinding used                | Not blinded                             |

## Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|   |   |
|---|---|
| <b>Arm title</b>  | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS |
| Arm description:  |   |
| Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2) |   |
| Arm type  | Experimental                                    |
| Investigational medicinal product name  | Ligelizumab                                     |
| Investigational medicinal product code  | QGE031  |
| Other name  |   |
| Pharmaceutical forms  | Solution for injection in pre-filled syringe    |
| Routes of administration  | Subcutaneous use                                |

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

|                  |   |
|------------------|---|
| <b>Arm title</b> | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS |
|------------------|---|

Arm description:

Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Ligelizumab                                  |
| Investigational medicinal product code | QGE031                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

Ligelizumab 120 mg pre-filled syringe (PFS) subcutaneously every 4 weeks (Q4W)

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS |
|---|---|---|
| Started   | 77  | 206   |
| Completed   | 1   | 2   |
| Not completed                                       | 76  | 204   |
| Subject decision                                    | 5   | 8   |
| Study terminated by sponsor                         | 71  | 195   |
| Lost to follow-up                                   | -   | 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: Not all subjects who completed the First half treatment period (TRT1) were eligible to start the second half treatment period (TRT2): Only participants with UAS7 > 6 and < 16 or with UAS7 ≥ 16 for whom the benefit-risk was deemed as positive by the investigator at Week 52 of TRT1 were transitioned to the TRT2 (ligelizumab 120 mg s.c. Q4W PFS) unless a decision to stop treatment was made based on a risk-benefit assessment.

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS |
|-----------------------|--|

Reporting group description:

Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

|                       |   |
|-----------------------|---|
| Reporting group title | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS |
|-----------------------|---|

Reporting group description:

Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)

| Reporting group values                             | Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS | Total |
|--|--|---|-------|
| Number of subjects                                 | 290  | 743   | 1033  |
| 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)                          | 11   | 29  | 40    |
| Adults (18-64 years)                               | 266  | 663   | 929   |
| From 65-84 years                                   | 13   | 51  | 64    |
| 85 years and over                                  | 0  | 0   | 0     |
| Age Continuous                                     |  |   |       |
| Units: Years                                       |  |   |       |
| arithmetic mean                                    | 42.4   | 42.8  | -     |
| standard deviation                                 | ± 13.98  | ± 14.40   | -     |
| Sex: Female, Male                                  |  |   |       |
| Units: Participants                                |  |   |       |
| Female   | 190  | 525   | 715   |
| Male   | 100  | 218   | 318   |
| Race/Ethnicity, Customized                         |  |   |       |
| Units: Subjects                                    |  |   |       |
| White  | 209  | 506   | 715   |
| Black or African American                          | 1  | 13  | 14    |
| Asian  | 66   | 199   | 265   |
| Native Hawaiian or Other Pacific Islander          | 0  | 1   | 1     |
| American Indian or Alaska Native                   | 11   | 20  | 31    |
| Multiple   | 3  | 4   | 7     |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Ligelizumab 72 mg LIVI -ligelizumab 120 mg PFS  |
| Reporting group description:<br>Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)  |   |
| Reporting group title  | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS |
| Reporting group description:<br>Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2) |   |
| Reporting group title  | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS |
| Reporting group description:<br>Participants received 72 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2)  |   |
| Reporting group title  | Ligelizumab 120 mg LIVI -ligelizumab 120 mg PFS |
| Reporting group description:<br>Participants received 120 mg of ligelizumab liquid in vial (LIVI), subcutaneously, every 4 weeks for the first 12 weeks. Thereafter, participants received 120 mg of ligelizumab pre-filled syringe (PFS), subcutaneously, every 4 weeks for up to 92 additional weeks (continuous or interrupted if the participant entered the observation period 2) |   |

### Primary: Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in the core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12

|   |   |
|---|---|
| End point title   | Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in the core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12 <sup>[1]</sup> |
| End point description:<br>The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity.<br>A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week.<br>The percentage of subjects transitioning from CQGE031C2302 and CQGE031C2303 and receiving the same dose regimen as in the core studies with UAS7 ≤ 6 at Week 12 was estimated using multiple imputation method. The 95% confidence interval was derived based on the Wilson score method with continuity correction. |   |
| End point type  | Primary   |
| End point timeframe:<br>Week 12 of the extension study  |   |
| Notes:<br>[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.<br>Justification: No statistical analyses were planned for this primary endpoint  |   |

|                                   |   |  |  |  |
|-----------------------------------|---|--|--|--|
| <b>End point values</b>           | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
| Subject group type                | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed       | 290   | 276  |  |  |
| Units: Percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 53.5 (48.72 to 58.54)                           | 57.5 (52.71 to 62.57)                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### **Primary: Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in core studies and who achieved UAS7 ≤ 6 at week 12 in core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12 of the extension study**

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303), receiving the same dose regimen as in core studies and who achieved UAS7 ≤ 6 at week 12 in core studies, with well-controlled disease (UAS7 ≤ 6) at Week 12 of the extension study <sup>[2]</sup> |
|-----------------|---|

End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals and the intensity of the pruritus over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity.

A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the UAS7 was missing for that week. Missing data was considered as non-responder.

The percentage of subjects transitioning from core studies (CQGE031C2302 and CQGE031C2303) and receiving the same dose regimen as in the core studies who achieved UAS7 ≤ 6 at week 12 in the core studies with UAS7 ≤ 6 at Week 12 of the extension study was estimated based on observed data.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Week 12 of the extension study

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were planned for this primary endpoint

|                                   |   |  |  |  |
|-----------------------------------|---|--|--|--|
| <b>End point values</b>           | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
| Subject group type                | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed       | 138   | 144  |  |  |
| Units: Percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 81.9 (74.73 to 87.92)                           | 82.6 (75.45 to 88.44)                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with completely controlled disease (UAS7 =0) at Week 12

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with completely controlled disease (UAS7 =0) at Week 12 |
|-----------------|---|

#### End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity.

A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week.

The percentage of subjects transitioning from core studies (CQGE031C2302 and CQGE031C2303) and receiving the same dose regimen as in the core studies with UAS7 = 0 at Week 12 was estimated using multiple imputation method.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

#### End point timeframe:

Week 12 of the extension study

| End point values                  | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed       | 290   | 276  |  |  |
| Units: Percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 37.3 (31.63 to 43.04)                           | 41.5 (35.61 to 47.36)                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from extension study baseline in the UAS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

|                 |  |
|-----------------|--|
| End point title | Change from extension study baseline in the UAS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies |
|-----------------|--|

#### End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7

indicated greater urticaria disease activity. A negative change score from extension study baseline indicates improvement.

A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week.

The absolute change from extension study baseline in the UAS7 at Week 12 was estimated using multiple imputation method.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Extension study baseline (Week 0), Week 12 of the extension study

| <b>End point values</b>          | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed      | 290   | 276  |  |  |
| Units: Score on a scale          |   |  |  |  |
| arithmetic mean (standard error) | -19.83 ( $\pm$ 13.12)                           | -20.41 ( $\pm$ 12.94)                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### **Secondary: Change from extension study baseline in the ISS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies**

|                 |  |
|-----------------|--|
| End point title | Change from extension study baseline in the ISS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies |
|-----------------|--|

End point description:

The Itch Severity Score (ISS) was recorded by the subject twice daily in their eDiary, on a scale of 0 (none) to 3 (intense/severe). A weekly score (ISS7) was derived by adding up the average daily scores of the 7 preceding days. The ISS7 ranged from 0 to 21. A higher ISS7 indicated more severe itching. A negative change score from baseline indicates improvement.

A minimum of 4 out of 7 daily scores were needed to calculate the ISS7 values. Otherwise, the weekly score was missing for that week.

The absolute change from extension study baseline in the ISS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies was estimated using multiple imputation method.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Extension study baseline (Week 0), Week 12 of the extension study

|                                  |   |  |  |  |
|----------------------------------|---|--|--|--|
| <b>End point values</b>          | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
| Subject group type               | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed      | 290   | 276  |  |  |
| Units: Score on a scale          |   |  |  |  |
| arithmetic mean (standard error) | -9.12 (± 6.35)                                  | -9.46 (± 6.55)                                   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from extension study baseline in the HSS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies

|                 |  |
|-----------------|--|
| End point title | Change from extension study baseline in the HSS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies |
|-----------------|--|

End point description:

The Hive Severity Score (HSS) was recorded by the subject twice daily in their eDiary, on a scale of 0 (none) to 3 (> 12 hives/12 hours). A weekly score (HSS7) was derived by adding up the average daily scores of the 7 preceding days. The HSS7 ranged from 0 to 21. A higher HSS7 indicated a greater number of hives. A negative change score from baseline indicates improvement.

A minimum of 4 out of 7 daily scores were needed to calculate the HSS7 values. Otherwise, the weekly score was missing for that week.

The absolute change from extension study baseline in the HSS7 at Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies was estimated using multiple imputation method.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Extension study baseline (Week 0), Week 12 of the extension study

|                                  |   |  |  |  |
|----------------------------------|---|--|--|--|
| <b>End point values</b>          | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
| Subject group type               | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed      | 290   | 276  |  |  |
| Units: Score on a scale          |   |  |  |  |
| arithmetic mean (standard error) | -10.71 (± 7.50)                                 | -10.95 (± 7.11)                                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects from core studies (CQGE031C2302 and

**CQGE031C2303) receiving the same dose regimen as in the core studies with DLQI = 0-1 at Week 12**

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with DLQI = 0-1 at Week 12 |
|-----------------|--|

## End point description:

The Dermatology Life Quality Index (DLQI) is a 10-item dermatology-specific quality of life (QoL) measure. Subjects rated their dermatology symptoms as well as the impact of their skin condition on various aspects of their lives thinking about the previous 7 days. An overall score was calculated and ranged from 0 to 30. Higher scores indicated worse disease-related QoL. A DLQI score of 0 or 1 indicated that there was no impact of a skin disease on the patient's life.

The percentage of subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies with DLQI = 0-1 at Week 12 was estimated using multiple imputation method.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

Week 12 of the extension study

| <b>End point values</b>           | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed       | 290   | 276  |  |  |
| Units: Percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 45.6 (39.66 to 51.52)                           | 55.8 (49.77 to 61.79)                            |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Cumulative number of angioedema-free weeks (AAS7=0) up to Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies**

|                 |  |
|-----------------|--|
| End point title | Cumulative number of angioedema-free weeks (AAS7=0) up to Week 12 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies |
|-----------------|--|

## End point description:

The Weekly angioedema activity score (AAS) is a validated tool to assess occurrence of episodes of angioedema. If the subject reported the occurrence of angioedema ("opening question") with "no", AAS score for this day was 0. If "yes" was the answer to the opening question, the subject continued to answer questions about the duration, severity and impact on daily functioning and appearance of the angioedema. A score between 0 and 3 was assigned to every answer field. The AAS7 was the weekly sum of the daily AAS. AAS7 scores ranged from 0-105. Higher score indicated more severe disease. AAS7 in all subjects from core studies (CQGE031C2302 and CQGE031C2303) receiving the same dose regimen as in the core studies was estimated using multiple imputation method. The imputed AAS7 = 0 was used for the cumulative number of weeks that subjects achieved AAS7 = 0 response calculation

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

From extension study baseline (Week 0) up to Week 12 of the extension study

|                                  |   |  |  |  |
|----------------------------------|---|--|--|--|
| <b>End point values</b>          | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
| Subject group type               | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed      | 290   | 276  |  |  |
| Units: Weeks                     |   |  |  |  |
| arithmetic mean (standard error) | 9.30 (± 0.25)                                   | 9.68 (± 0.27)                                    |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects with well-controlled disease (UAS7 ≤ 6) 12 weeks after starting self-administration

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with well-controlled disease (UAS7 ≤ 6) 12 weeks after starting self-administration |
|-----------------|--|

End point description:

The Urticaria Activity Score (UAS) is a composite, diary-recorded score with numeric severity intensity ratings (0=none to 3=intense/severe) for the number of wheals (hives) and the intensity of the pruritus (itch) over the past 12 hours (twice daily). The daily UAS is calculated as the average of the morning and evening scores. The UAS7 is the weekly sum of the daily UAS, which is the composite score of the intensity of pruritus and the number of wheals. UAS7 scores ranged from 0 to 42. A higher UAS7 indicated greater urticaria disease activity.

A minimum of 4 out of 7 daily scores were needed to calculate the UAS7 values. Otherwise, the weekly score was missing for that week. Missing data was considered as non-responder in the analysis. The percentage of subjects with UAS7 ≤ 6 at Week 24 (i.e., 12 weeks after starting self-administration) was estimated based on observed data.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Week 24 of the extension study

|                                   |   |  |  |  |
|-----------------------------------|---|--|--|--|
| <b>End point values</b>           | Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS | Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |  |  |
| Subject group type                | Reporting group                                 | Reporting group                                  |  |  |
| Number of subjects analysed       | 153   | 383  |  |  |
| Units: Percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 69.4 (60.86 to 77.07)                           | 69.5 (64.40 to 74.21)                            |  |  |

## Statistical analyses

---

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

TAEs were assessed from first dose to 16 weeks post-last dose of each period (listed below) or entire study (up to 2.5 years): TRT1A: Within the first 12 weeks of treatment ; TRT1B: From Week 12 to 52 of treatment; TRT2: From Week 52 to 104 of treatment

Adverse event reporting additional description:

Treatment-emergent AEs (TEAEs): events started after the first dose within 16 weeks of last dose of study treatment, or pre-existing events that increased in severity within 16 weeks after the last dose. TEAEs counted for each treatment period were those with onset after the start of the treatment period or worsening within that period.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

### Reporting groups

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | TRT1A Ligelizumab 72 mg LIVI |
|-----------------------|------------------------------|

Reporting group description:

AEs collected during the TRT1A period. During this period, participants received 72 mg of ligelizumab LIVI, subcutaneously, every 4 weeks for the first 12 weeks.

|                       |             |
|-----------------------|-------------|
| Reporting group title | TRT1A Total |
|-----------------------|-------------|

Reporting group description:

AEs collected during the TRT1A period.

|                       |   |
|-----------------------|---|
| Reporting group title | TRT1B Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS |
|-----------------------|---|

Reporting group description:

AEs collected during the TRT1B period. During this period, participants previously treated with ligelizumab 72 mg LIVI received 120 mg of ligelizumab PFS, subcutaneously, every 4 weeks from Week 12 to Week 52

|                       |  |
|-----------------------|--|
| Reporting group title | TRT1B Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |
|-----------------------|--|

Reporting group description:

AEs collected during the TRT1B period. During this period, participants previously treated with ligelizumab 120 mg LIVI received 120 mg of ligelizumab PFS, subcutaneously, every 4 weeks from Week 12 to Week 52.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Entire study Total |
|-----------------------|--------------------|

Reporting group description:

AEs collected from first dose of study treatment to 16 weeks of last dose of study treatment.

|                       |  |
|-----------------------|--|
| Reporting group title | TRT2 Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS |
|-----------------------|--|

Reporting group description:

AEs collected during the TRT2 period. During this period, participants previously treated with ligelizumab 72 mg LIVI received 120 mg of ligelizumab PFS, subcutaneously, every 4 weeks for up to 52 weeks

|                       |   |
|-----------------------|---|
| Reporting group title | TRT2 Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |
|-----------------------|---|

Reporting group description:

AEs collected during the TRT2 period. During this period, participants previously treated with ligelizumab 120 mg LIVI received 120 mg of ligelizumab PFS, subcutaneously, every 4 weeks for up to 52 weeks

|                       |            |
|-----------------------|------------|
| Reporting group title | TRT2 Total |
|-----------------------|------------|

Reporting group description:

AEs collected during the TRT2 period

|                       |  |
|-----------------------|--|
| Reporting group title | Entire study Ligelizumab 72 mg LIVI - ligelizumab 120 mg PFS |
|-----------------------|--|

Reporting group description:

AEs collected from first dose of study treatment to 16 weeks of last dose of study treatment

|                       |   |
|-----------------------|---|
| Reporting group title | Entire study Ligelizumab 120 mg LIVI - ligelizumab 120 mg PFS |
|-----------------------|---|

Reporting group description:

AEs collected from first dose of study treatment to 16 weeks of last dose of study treatment

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | TRT1A Ligelizumab 120 mg LIVI |
|-----------------------|-------------------------------|

Reporting group description:

AEs collected during the TRT1A period. During this period, participants received 120 mg of ligelizumab LIVI, subcutaneously, every 4 weeks for the first 12 week

|                       |             |
|-----------------------|-------------|
| Reporting group title | TRT1B Total |
|-----------------------|-------------|

Reporting group description:

AEs collected during the TRT1B period

| <b>Serious adverse events</b>                                       | TRT1A Ligelizumab<br>72 mg LIVI | TRT1A Total       | TRT1B Ligelizumab<br>72 mg LIVI -<br>ligelizumab 120 mg<br>PFS |
|---|---------------------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                                 |                   |  |
| subjects affected / exposed   | 1 / 288 (0.35%)                 | 11 / 1033 (1.06%) | 5 / 263 (1.90%)  |
| number of deaths (all causes)                                       | 0                               | 0                 | 0  |
| number of deaths resulting from adverse events                      | 0                               | 0                 | 0  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                 |                   |  |
| Breast cancer   |                                 |                   |  |
| subjects affected / exposed   | 0 / 288 (0.00%)                 | 0 / 1033 (0.00%)  | 0 / 263 (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  |
| Endometrial cancer  |                                 |                   |  |
| subjects affected / exposed   | 0 / 288 (0.00%)                 | 0 / 1033 (0.00%)  | 0 / 263 (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  |
| Oral neoplasm   |                                 |                   |  |
| subjects affected / exposed   | 0 / 288 (0.00%)                 | 1 / 1033 (0.10%)  | 0 / 263 (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  |
| Pancreatic carcinoma  |                                 |                   |  |
| subjects affected / exposed   | 0 / 288 (0.00%)                 | 0 / 1033 (0.00%)  | 0 / 263 (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  |
| Papillary thyroid cancer  |                                 |                   |  |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed                          | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Testis cancer  |                 |                  |                 |
| subjects affected / exposed                          | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Uterine leiomyoma                                    |                 |                  |                 |
| subjects affected / exposed                          | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Vascular disorders                                   |                 |                  |                 |
| Hypertension   |                 |                  |                 |
| subjects affected / exposed                          | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 1 / 263 (0.38%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            | 0 / 0           |
| General disorders and administration site conditions |                 |                  |                 |
| Drowning   |                 |                  |                 |
| subjects affected / exposed                          | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Chest pain   |                 |                  |                 |
| subjects affected / exposed                          | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Fatigue  |                 |                  |                 |
| subjects affected / exposed                          | 1 / 288 (0.35%) | 1 / 1033 (0.10%) | 0 / 263 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0            | 0 / 0           |
| Immune system disorders                              |                 |                  |                 |
| Anaphylactic reaction                                |                 |                  |                 |
| subjects affected / exposed                          | 0 / 288 (0.00%) | 1 / 1033 (0.10%) | 0 / 263 (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           |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| Reproductive system and breast disorders        |                 |                  |                 |
| Abnormal uterine bleeding                       |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Intermenstrual bleeding                         |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Sleep apnoea syndrome                           |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Pneumothorax spontaneous                        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Pulmonary embolism                              |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 1 / 263 (0.38%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Psychiatric disorders                           |                 |                  |                 |
| Suicide attempt                                 |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Injury, poisoning and procedural complications  |                 |                  |                 |
| Animal bite                                     |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 288 (0.00%) | 1 / 1033 (0.10%) | 0 / 263 (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>Comminuted fracture</b>                      |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Hand fracture</b>                            |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Meniscus injury</b>                          |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Wrist fracture</b>                           |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Cardiac disorders</b>                        |                 |                  |                 |
| <b>Congestive cardiomyopathy</b>                |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 1 / 1033 (0.10%) | 0 / 263 (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>Mitral valve incompetence</b>                |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 1 / 1033 (0.10%) | 0 / 263 (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>Myocardial ischaemia</b>                     |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Nervous system disorders</b>                 |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| Loss of consciousness                           |                 |                  |                 |
| subjects affected / exposed                     | 1 / 288 (0.35%) | 1 / 1033 (0.10%) | 0 / 263 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Headache  |                 |                  |                 |
| subjects affected / exposed                     | 1 / 288 (0.35%) | 1 / 1033 (0.10%) | 0 / 263 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Vascular encephalopathy                         |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Ear and labyrinth disorders                     |                 |                  |                 |
| Meniere's disease                               |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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                      |                 |                  |                 |
| Nausea  |                 |                  |                 |
| subjects affected / exposed                     | 1 / 288 (0.35%) | 1 / 1033 (0.10%) | 0 / 263 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Vomiting  |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Hepatobiliary disorders                         |                 |                  |                 |
| Biliary dilatation                              |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Cholecystitis acute                             |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed                            | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 1 / 263 (0.38%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Cholestasis</b>                                     |                 |                  |                 |
| subjects affected / exposed                            | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Hyperbilirubinaemia</b>                             |                 |                  |                 |
| subjects affected / exposed                            | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Skin and subcutaneous tissue disorders</b>          |                 |                  |                 |
| <b>Chronic spontaneous urticaria</b>                   |                 |                  |                 |
| subjects affected / exposed                            | 0 / 288 (0.00%) | 1 / 1033 (0.10%) | 0 / 263 (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>Renal and urinary disorders</b>                     |                 |                  |                 |
| <b>Nephrolithiasis</b>                                 |                 |                  |                 |
| subjects affected / exposed                            | 0 / 288 (0.00%) | 2 / 1033 (0.19%) | 0 / 263 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Ureterolithiasis</b>                                |                 |                  |                 |
| subjects affected / exposed                            | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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>Musculoskeletal and connective tissue disorders</b> |                 |                  |                 |
| <b>Neck pain</b>                                       |                 |                  |                 |
| subjects affected / exposed                            | 1 / 288 (0.35%) | 1 / 1033 (0.10%) | 0 / 263 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Intervertebral disc protrusion</b>                  |                 |                  |                 |
| subjects affected / exposed                            | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| Spinal stenosis                                 |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Polyarthritis                                   |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Infections and infestations                     |                 |                  |                 |
| Peritonitis                                     |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Diverticulitis                                  |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| Chronic tonsillitis                             |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 0 / 263 (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           |
| COVID-19  |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 2 / 1033 (0.19%) | 1 / 263 (0.38%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Pneumonia                                       |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 0 / 1033 (0.00%) | 1 / 263 (0.38%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Pharyngitis                                     |                 |                  |                 |
| subjects affected / exposed                     | 0 / 288 (0.00%) | 1 / 1033 (0.10%) | 0 / 263 (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>  | TRT1B Ligelizumab<br>120 mg LIVI -<br>ligelizumab 120 mg<br>PFS | Entire study Total | TRT2 Ligelizumab 72<br>mg LIVI -<br>ligelizumab 120 mg<br>PFS |
|--|---|--------------------|---|
| Total subjects affected by serious<br>adverse events                   |   |                    |   |
| subjects affected / exposed  | 32 / 684 (4.68%)  | 52 / 1033 (5.03%)  | 2 / 77 (2.60%)  |
| number of deaths (all causes)  | 3   | 3                  | 0   |
| number of deaths resulting from<br>adverse events                      | 0   | 0                  | 0   |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |   |                    |   |
| Breast cancer  |   |                    |   |
| subjects affected / exposed  | 1 / 684 (0.15%)   | 1 / 1033 (0.10%)   | 0 / 77 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 1   | 0 / 1              | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 0   | 0 / 0              | 0 / 0   |
| Endometrial cancer   |   |                    |   |
| subjects affected / exposed  | 1 / 684 (0.15%)   | 1 / 1033 (0.10%)   | 0 / 77 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 1   | 0 / 1              | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 0   | 0 / 0              | 0 / 0   |
| Oral neoplasm  |   |                    |   |
| subjects affected / exposed  | 0 / 684 (0.00%)   | 1 / 1033 (0.10%)   | 0 / 77 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 0   | 0 / 1              | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 0   | 0 / 0              | 0 / 0   |
| Pancreatic carcinoma   |   |                    |   |
| subjects affected / exposed  | 1 / 684 (0.15%)   | 1 / 1033 (0.10%)   | 0 / 77 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 1   | 0 / 1              | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 1   | 0 / 1              | 0 / 0   |
| Papillary thyroid cancer   |   |                    |   |
| subjects affected / exposed  | 1 / 684 (0.15%)   | 1 / 1033 (0.10%)   | 0 / 77 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 1   | 0 / 1              | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 0   | 0 / 0              | 0 / 0   |
| Testis cancer  |   |                    |   |
| subjects affected / exposed  | 1 / 684 (0.15%)   | 1 / 1033 (0.10%)   | 0 / 77 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 1   | 0 / 1              | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 0   | 0 / 0              | 0 / 0   |
| Uterine leiomyoma  |   |                    |   |

|   |                 |                  |                |
|---|-----------------|------------------|----------------|
| subjects affected / exposed                                 | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all             | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Vascular disorders</b>                                   |                 |                  |                |
| Hypertension  |                 |                  |                |
| subjects affected / exposed                                 | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>General disorders and administration site conditions</b> |                 |                  |                |
| Drowning  |                 |                  |                |
| subjects affected / exposed                                 | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all             | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 1           | 0 / 1            | 0 / 0          |
| Chest pain  |                 |                  |                |
| subjects affected / exposed                                 | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 1            | 0 / 1          |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0            | 0 / 0          |
| Fatigue   |                 |                  |                |
| subjects affected / exposed                                 | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Immune system disorders</b>                              |                 |                  |                |
| Anaphylactic reaction                                       |                 |                  |                |
| subjects affected / exposed                                 | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Reproductive system and breast disorders</b>             |                 |                  |                |
| Abnormal uterine bleeding                                   |                 |                  |                |
| subjects affected / exposed                                 | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all             | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0            | 0 / 0          |
| Intermenstrual bleeding                                     |                 |                  |                |

|  |                 |                  |                |
|--|-----------------|------------------|----------------|
| subjects affected / exposed                            | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Respiratory, thoracic and mediastinal disorders</b> |                 |                  |                |
| Asthma   |                 |                  |                |
| subjects affected / exposed                            | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0          |
| Sleep apnoea syndrome                                  |                 |                  |                |
| subjects affected / exposed                            | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0          |
| Pneumothorax spontaneous                               |                 |                  |                |
| subjects affected / exposed                            | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0          |
| Pulmonary embolism                                     |                 |                  |                |
| subjects affected / exposed                            | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Psychiatric disorders</b>                           |                 |                  |                |
| Suicide attempt  |                 |                  |                |
| subjects affected / exposed                            | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Injury, poisoning and procedural complications</b>  |                 |                  |                |
| Animal bite  |                 |                  |                |
| subjects affected / exposed                            | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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          |
| Comminuted fracture                                    |                 |                  |                |

|   |                 |                  |                |
|---|-----------------|------------------|----------------|
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Hand fracture</b>                            |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Meniscus injury</b>                          |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Wrist fracture</b>                           |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Cardiac disorders</b>                        |                 |                  |                |
| <b>Congestive cardiomyopathy</b>                |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Mitral valve incompetence</b>                |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Myocardial ischaemia</b>                     |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Nervous system disorders</b>                 |                 |                  |                |
| <b>Loss of consciousness</b>                    |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Headache</b>                                 |                 |                  |                |

|   |                 |                  |                |
|---|-----------------|------------------|----------------|
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Vascular encephalopathy</b>                  |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Ear and labyrinth disorders</b>              |                 |                  |                |
| <b>Meniere's disease</b>                        |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Gastrointestinal disorders</b>               |                 |                  |                |
| <b>Nausea</b>                                   |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Vomiting</b>                                 |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Hepatobiliary disorders</b>                  |                 |                  |                |
| <b>Biliary dilatation</b>                       |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| <b>Cholecystitis acute</b>                      |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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>Cholestasis</b>                              |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |

|   |                 |                  |                |
|---|-----------------|------------------|----------------|
| Hyperbilirubinaemia                             |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                 |                  |                |
| Chronic spontaneous urticaria                   |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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          |
| Renal and urinary disorders                     |                 |                  |                |
| Nephrolithiasis                                 |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 2 / 1033 (0.19%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| Ureterolithiasis                                |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                 |                  |                |
| Neck pain                                       |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 0 / 77 (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          |
| Intervertebral disc protrusion                  |                 |                  |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| Spinal stenosis                                 |                 |                  |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%) | 1 / 77 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0          |
| Polyarthritis                                   |                 |                  |                |

|   |                 |                   |                |
|---|-----------------|-------------------|----------------|
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%)  | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1             | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0          |
| <b>Infections and infestations</b>              |                 |                   |                |
| <b>Peritonitis</b>                              |                 |                   |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%)  | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1             | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0          |
| <b>Diverticulitis</b>                           |                 |                   |                |
| subjects affected / exposed                     | 2 / 684 (0.29%) | 2 / 1033 (0.19%)  | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2             | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0          |
| <b>Chronic tonsillitis</b>                      |                 |                   |                |
| subjects affected / exposed                     | 1 / 684 (0.15%) | 1 / 1033 (0.10%)  | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1             | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0          |
| <b>COVID-19</b>                                 |                 |                   |                |
| subjects affected / exposed                     | 7 / 684 (1.02%) | 12 / 1033 (1.16%) | 0 / 77 (0.00%) |
| occurrences causally related to treatment / all | 0 / 7           | 0 / 12            | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1             | 0 / 0          |
| <b>Pneumonia</b>                                |                 |                   |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%)  | 0 / 77 (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>Pharyngitis</b>                              |                 |                   |                |
| subjects affected / exposed                     | 0 / 684 (0.00%) | 1 / 1033 (0.10%)  | 0 / 77 (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>                     | TRT2 Ligelizumab<br>120 mg LIVI -<br>ligelizumab 120 mg<br>PFS | TRT2 Total      | Entire study<br>Ligelizumab 72 mg<br>LIVI - ligelizumab<br>120 mg PFS |
|---|--|-----------------|---|
| Total subjects affected by serious adverse events |  |                 |   |
| subjects affected / exposed                       | 3 / 206 (1.46%)  | 5 / 283 (1.77%) | 8 / 288 (2.78%)   |
| number of deaths (all causes)                     | 0  | 0               | 0   |

| number of deaths resulting from adverse events                      | 0               | 0               | 0               |
|---|-----------------|-----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Breast cancer   |                 |                 |                 |
| subjects affected / exposed   | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Endometrial cancer  |                 |                 |                 |
| subjects affected / exposed   | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Oral neoplasm   |                 |                 |                 |
| subjects affected / exposed   | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Pancreatic carcinoma  |                 |                 |                 |
| subjects affected / exposed   | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Papillary thyroid cancer  |                 |                 |                 |
| subjects affected / exposed   | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Testis cancer   |                 |                 |                 |
| subjects affected / exposed   | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Uterine leiomyoma   |                 |                 |                 |
| subjects affected / exposed   | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Vascular disorders  |                 |                 |                 |
| Hypertension  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                                 | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>General disorders and administration site conditions</b> |                 |                 |                 |
| <b>Drowning</b>   |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Chest pain</b>   |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 206 (0.00%) | 1 / 283 (0.35%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Fatigue</b>  |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all                  | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Immune system disorders</b>                              |                 |                 |                 |
| <b>Anaphylactic reaction</b>                                |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Reproductive system and breast disorders</b>             |                 |                 |                 |
| <b>Abnormal uterine bleeding</b>                            |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Intermenstrual bleeding</b>                              |                 |                 |                 |
| subjects affected / exposed                                 | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Respiratory, thoracic and mediastinal disorders</b>      |                 |                 |                 |
| <b>Asthma</b>   |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Sleep apnoea syndrome</b>                          |                 |                 |                 |
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Pneumothorax spontaneous</b>                       |                 |                 |                 |
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Pulmonary embolism</b>                             |                 |                 |                 |
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Psychiatric disorders</b>                          |                 |                 |                 |
| <b>Suicide attempt</b>                                |                 |                 |                 |
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Injury, poisoning and procedural complications</b> |                 |                 |                 |
| <b>Animal bite</b>                                    |                 |                 |                 |
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Comminuted fracture</b>                            |                 |                 |                 |
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Hand fracture</b>                                  |                 |                 |                 |
| subjects affected / exposed                           | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Meniscus injury                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Wrist fracture                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Cardiac disorders                               |                 |                 |                 |
| Congestive cardiomyopathy                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Mitral valve incompetence                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Myocardial ischaemia                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Nervous system disorders                        |                 |                 |                 |
| Loss of consciousness                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Headache  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vascular encephalopathy                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Ear and labyrinth disorders                     |                 |                 |                 |
| Meniere's disease                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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                      |                 |                 |                 |
| Nausea  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vomiting  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 206 (0.49%) | 1 / 283 (0.35%) | 0 / 288 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                 |                 |                 |
| Biliary dilatation                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Cholecystitis acute                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cholestasis                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Hyperbilirubinaemia                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Skin and subcutaneous tissue disorders          |                 |                 |                 |
| Chronic spontaneous urticaria                   |                 |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                            | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Renal and urinary disorders</b>                     |                 |                 |                 |
| <b>Nephrolithiasis</b>                                 |                 |                 |                 |
| subjects affected / exposed                            | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Ureterolithiasis</b>                                |                 |                 |                 |
| subjects affected / exposed                            | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Musculoskeletal and connective tissue disorders</b> |                 |                 |                 |
| <b>Neck pain</b>                                       |                 |                 |                 |
| subjects affected / exposed                            | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Intervertebral disc protrusion</b>                  |                 |                 |                 |
| subjects affected / exposed                            | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Spinal stenosis</b>                                 |                 |                 |                 |
| subjects affected / exposed                            | 0 / 206 (0.00%) | 1 / 283 (0.35%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all        | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all             | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Polyarthritis</b>                                   |                 |                 |                 |
| subjects affected / exposed                            | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>Infections and infestations</b>                     |                 |                 |                 |
| <b>Peritonitis</b>                                     |                 |                 |                 |
| subjects affected / exposed                            | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Diverticulitis                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| Chronic tonsillitis                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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           |
| COVID-19  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 206 (0.97%) | 2 / 283 (0.71%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 1 / 288 (0.35%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pharyngitis                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 206 (0.00%) | 0 / 283 (0.00%) | 0 / 288 (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>                                       | Entire study<br>Ligelizumab 120 mg<br>LIVI - ligelizumab<br>120 mg PFS | TRT1A Ligelizumab<br>120 mg LIVI | TRT1B Total      |
|---|--|----------------------------------|------------------|
| Total subjects affected by serious adverse events                   |  |                                  |                  |
| subjects affected / exposed   | 44 / 745 (5.91%)   | 10 / 745 (1.34%)                 | 37 / 947 (3.91%) |
| number of deaths (all causes)                                       | 3  | 0                                | 3                |
| number of deaths resulting from adverse events                      | 0  | 0                                | 0                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |                                  |                  |
| Breast cancer   |  |                                  |                  |
| subjects affected / exposed   | 1 / 745 (0.13%)  | 0 / 745 (0.00%)                  | 1 / 947 (0.11%)  |
| occurrences causally related to treatment / all                     | 0 / 1  | 0 / 0                            | 0 / 1            |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0                            | 0 / 0            |
| Endometrial cancer  |  |                                  |                  |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Oral neoplasm  |                 |                 |                 |
| subjects affected / exposed                          | 1 / 745 (0.13%) | 1 / 745 (0.13%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Pancreatic carcinoma                                 |                 |                 |                 |
| subjects affected / exposed                          | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           | 0 / 1           |
| Papillary thyroid cancer                             |                 |                 |                 |
| subjects affected / exposed                          | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Testis cancer  |                 |                 |                 |
| subjects affected / exposed                          | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Uterine leiomyoma                                    |                 |                 |                 |
| subjects affected / exposed                          | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Vascular disorders                                   |                 |                 |                 |
| Hypertension   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| General disorders and administration site conditions |                 |                 |                 |
| Drowning   |                 |                 |                 |
| subjects affected / exposed                          | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           | 0 / 1           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Chest pain                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 0 / 947 (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           |
| Fatigue   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 0 / 947 (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           |
| Immune system disorders                         |                 |                 |                 |
| Anaphylactic reaction                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 1 / 745 (0.13%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders        |                 |                 |                 |
| Abnormal uterine bleeding                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Intermenstrual bleeding                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 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                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Sleep apnoea syndrome                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumothorax spontaneous                        |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                           | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Pulmonary embolism</b>                             |                 |                 |                 |
| subjects affected / exposed                           | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all       | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Psychiatric disorders</b>                          |                 |                 |                 |
| <b>Suicide attempt</b>                                |                 |                 |                 |
| subjects affected / exposed                           | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Injury, poisoning and procedural complications</b> |                 |                 |                 |
| <b>Animal bite</b>                                    |                 |                 |                 |
| subjects affected / exposed                           | 1 / 745 (0.13%) | 1 / 745 (0.13%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Comminuted fracture</b>                            |                 |                 |                 |
| subjects affected / exposed                           | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Hand fracture</b>                                  |                 |                 |                 |
| subjects affected / exposed                           | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Meniscus injury</b>                                |                 |                 |                 |
| subjects affected / exposed                           | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |
| <b>Wrist fracture</b>                                 |                 |                 |                 |
| subjects affected / exposed                           | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all       | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Cardiac disorders                               |                 |                 |                 |
| Congestive cardiomyopathy                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 1 / 745 (0.13%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Mitral valve incompetence                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 1 / 745 (0.13%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Myocardial ischaemia                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Loss of consciousness                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 0 / 947 (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           |
| Headache  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 0 / 947 (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           |
| Vascular encephalopathy                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ear and labyrinth disorders                     |                 |                 |                 |
| Meniere's disease                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Nausea  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 0 / 947 (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           |
| Vomiting  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                 |                 |                 |
| Biliary dilatation                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cholecystitis acute                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cholestasis                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyperbilirubinaemia                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                 |                 |                 |
| Chronic spontaneous urticaria                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 1 / 745 (0.13%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Nephrolithiasis                                 |                 |                 |                 |
| subjects affected / exposed                     | 2 / 745 (0.27%) | 2 / 745 (0.27%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Ureterolithiasis                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Neck pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 0 / 947 (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           |
| Intervertebral disc protrusion                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal stenosis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%) | 0 / 745 (0.00%) | 0 / 947 (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           |
| Polyarthritis                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Peritonitis                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Diverticulitis                                  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 745 (0.27%) | 0 / 745 (0.00%) | 2 / 947 (0.21%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Chronic tonsillitis                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%) | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                  |                 |                 |
|---|------------------|-----------------|-----------------|
| COVID-19  |                  |                 |                 |
| subjects affected / exposed                     | 11 / 745 (1.48%) | 2 / 745 (0.27%) | 8 / 947 (0.84%) |
| occurrences causally related to treatment / all | 0 / 11           | 0 / 2           | 0 / 8           |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0           | 0 / 1           |
| Pneumonia                                       |                  |                 |                 |
| subjects affected / exposed                     | 0 / 745 (0.00%)  | 0 / 745 (0.00%) | 1 / 947 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0           | 0 / 0           |
| Pharyngitis                                     |                  |                 |                 |
| subjects affected / exposed                     | 1 / 745 (0.13%)  | 1 / 745 (0.13%) | 0 / 947 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0           | 0 / 0           |

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

| <b>Non-serious adverse events</b>                     | TRT1A Ligelizumab<br>72 mg LIVI | TRT1A Total       | TRT1B Ligelizumab<br>72 mg LIVI -<br>ligelizumab 120 mg<br>PFS |
|---|---------------------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                                 |                   |  |
| subjects affected / exposed                           | 12 / 288 (4.17%)                | 77 / 1033 (7.45%) | 49 / 263 (18.63%)  |
| Nervous system disorders                              |                                 |                   |  |
| Headache  |                                 |                   |  |
| subjects affected / exposed                           | 4 / 288 (1.39%)                 | 30 / 1033 (2.90%) | 13 / 263 (4.94%)   |
| occurrences (all)                                     | 10                              | 42                | 21   |
| General disorders and administration site conditions  |                                 |                   |  |
| Pyrexia   |                                 |                   |  |
| subjects affected / exposed                           | 2 / 288 (0.69%)                 | 12 / 1033 (1.16%) | 5 / 263 (1.90%)  |
| occurrences (all)                                     | 2                               | 12                | 6  |
| Infections and infestations                           |                                 |                   |  |
| Nasopharyngitis                                       |                                 |                   |  |
| subjects affected / exposed                           | 3 / 288 (1.04%)                 | 19 / 1033 (1.84%) | 8 / 263 (3.04%)  |
| occurrences (all)                                     | 3                               | 19                | 8  |
| COVID-19  |                                 |                   |  |
| subjects affected / exposed                           | 4 / 288 (1.39%)                 | 24 / 1033 (2.32%) | 28 / 263 (10.65%)  |
| occurrences (all)                                     | 4                               | 24                | 31   |

| <b>Non-serious adverse events</b>  | TRT1B Ligelizumab<br>120 mg LIVI -<br>ligelizumab 120 mg<br>PFS | Entire study Total   | TRT2 Ligelizumab 72<br>mg LIVI -<br>ligelizumab 120 mg<br>PFS |
|--|---|--|---|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed  | 156 / 684 (22.81%)  | 289 / 1033<br>(27.98%)                                       | 11 / 77 (14.29%)  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 43 / 684 (6.29%)<br>94  | 81 / 1033 (7.84%)<br>178                                     | 5 / 77 (6.49%)<br>8   |
| General disorders and administration<br>site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 26 / 684 (3.80%)<br>27  | 46 / 1033 (4.45%)<br>53                                      | 0 / 77 (0.00%)<br>0   |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>COVID-19<br>subjects affected / exposed<br>occurrences (all) | 37 / 684 (5.41%)<br>51<br><br>78 / 684 (11.40%)<br>78           | 68 / 1033 (6.58%)<br>89<br><br>155 / 1033<br>(15.00%)<br>160 | 2 / 77 (2.60%)<br>2<br><br>6 / 77 (7.79%)<br>6                |

| <b>Non-serious adverse events</b>  | TRT2 Ligelizumab<br>120 mg LIVI -<br>ligelizumab 120 mg<br>PFS | TRT2 Total             | Entire study<br>Ligelizumab 72 mg<br>LIVI - ligelizumab<br>120 mg PFS |
|--|--|------------------------|---|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed                                | 36 / 206 (17.48%)  | 47 / 283 (16.61%)      | 65 / 288 (22.57%)   |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                               | 6 / 206 (2.91%)<br>13  | 11 / 283 (3.89%)<br>21 | 17 / 288 (5.90%)<br>39  |
| General disorders and administration<br>site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all) | 5 / 206 (2.43%)<br>8   | 5 / 283 (1.77%)<br>8   | 7 / 288 (2.43%)<br>8  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>COVID-19     | 7 / 206 (3.40%)<br>9   | 9 / 283 (3.18%)<br>11  | 12 / 288 (4.17%)<br>13  |

|                             |                   |                  |                   |
|-----------------------------|-------------------|------------------|-------------------|
| subjects affected / exposed | 21 / 206 (10.19%) | 27 / 283 (9.54%) | 38 / 288 (13.19%) |
| occurrences (all)           | 21                | 27               | 41                |

| <b>Non-serious adverse events</b>                     | Entire study<br>Ligelizumab 120 mg<br>LIVI - ligelizumab<br>120 mg PFS | TRT1A Ligelizumab<br>120 mg LIVI | TRT1B Total        |
|---|--|----------------------------------|--------------------|
| Total subjects affected by non-serious adverse events |  |                                  |                    |
| subjects affected / exposed                           | 224 / 745 (30.07%)   | 65 / 745 (8.72%)                 | 205 / 947 (21.65%) |
| Nervous system disorders                              |  |                                  |                    |
| Headache  |  |                                  |                    |
| subjects affected / exposed                           | 64 / 745 (8.59%)   | 26 / 745 (3.49%)                 | 56 / 947 (5.91%)   |
| occurrences (all)                                     | 139  | 32                               | 115                |
| General disorders and administration site conditions  |  |                                  |                    |
| Pyrexia   |  |                                  |                    |
| subjects affected / exposed                           | 39 / 745 (5.23%)   | 10 / 745 (1.34%)                 | 31 / 947 (3.27%)   |
| occurrences (all)                                     | 45   | 10                               | 33                 |
| Infections and infestations                           |  |                                  |                    |
| Nasopharyngitis                                       |  |                                  |                    |
| subjects affected / exposed                           | 56 / 745 (7.52%)   | 16 / 745 (2.15%)                 | 45 / 947 (4.75%)   |
| occurrences (all)                                     | 76   | 16                               | 59                 |
| COVID-19  |  |                                  |                    |
| subjects affected / exposed                           | 117 / 745 (15.70%)   | 20 / 745 (2.68%)                 | 106 / 947 (11.19%) |
| occurrences (all)                                     | 119  | 20                               | 109                |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment   |
|---------------|---|
| 09 April 2021 | The amendment primarily aimed to introduce measures to allow more flexibility to the subjects successfully completing one of the preceding studies to be able to continue receiving investigational treatment. These measures included allowance of a limited amount of missing e-diary entries prior to the first treatment visit and ensuring exclusion criteria and prohibited medications were not more stringent than the original preceding study's criteria.<br>Further, the original compliance criteria for eDiary HSS and ISS entries in the week prior to the Week 52 visit were removed. In case subjects did not meet full compliance with eDiary entries, the subjects could be moved to the second observation period; however, it was more appropriate for the subjects to be allowed to continue treatment even in the case of some missing eDiary entries as long as the UAS7 score was calculable as per the definition. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, disposition in OBS2 and follow-up could not be added. Please use <https://www.novctrd.com/>

Notes: